The American Society of Hospital Pharmacists, an affiliate of the American Pharmaceutical Association, is a national organization devoted to the profession of hospital pharmacy and dedicated to the improvement of pharmaceutical service in the interest of better patient care in hospitals.

MEMBERSHIP in the American Society of Hospital Pharmacists and the American Pharmaceutical Association is open to all practicing hospital pharmacists. With membership are included subscriptions to the American Journal of Hospital Pharmacy and to the *Journal* of the American Pharmaceutical Association, Pract. Pharm. Ed., as well as the several services of each organization.

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American Journal of Hospital Pharmacy

American Society of Hospital Pharmacists

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articles

departments

DEDICATION TO HARVEY A. K. WHITNEY

1894-1957

► THIS FIRST ISSUE of the AMERICAN JOURNAL OF HOSPITAL PHARMACY is dedicated to Harvey A. K. Whitney, founder and first President (Chairman) of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, who died on December 15, 1957 at the age of 63. Mr. Whitney died at the University Hospital in Ann Arbor, Michigan, the place which was a second home to him. His death was sudden. He had entered the hospital December 2, was operated on December 5 for an abdominal aneurysm, and died 10 days later following postoperative complications. He lies buried in Ann Arbor, survived by his wife Hildreth Whitney, his son Harvey Whitney, Jr. who is a junior student in the College of Pharmacy of the University of Michigan, his daughter Joan Whitney Braly, his brother Arthur of Adrian, and his sister Mrs. Gladys Woods of Fort Lauderdale, Florida.

Mr. Whitney will be long remembered as an inspiring leader in hospital pharmacy. Undoubtedly, his greatest contribution was to mold an obscure and unrecognized group of professional practitioners into a well-organized professional society. Under his dynamic leadership the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS was conceived, born, and nurtured, its principles dedicated to service for the patient, its objectives directed to stimulating hospital pharmacists to better prepare for this service through the improvement of standards of practice, of education and of training, and through the promotion of research and the dissemination of knowledge. The success of Harvey Whitney's inspirational leadership is characterized in the words of the eminent historian, Dr. George Urdang, who in 1952 wrote:

> "Today, American hospital pharmacy represents a unit of purpose and ideals second to none in the world in its willingness to achieve and maintain the highest educational standards possible and to be equal to whatever task the rapid progress of science and technic may offer to the pharmaceutical expert in the various fields of his professional advance."

The second contribution for which Mr. Whitney will be long remembered is his pioneering work in the establishment of hospital pharmacy internships in the United States. He began the first internship program at the University Hospital, University of Michigan, in 1927. In this work Mr. Whitney was far ahead of his time. It was to be more than a decade before the first combined internship and graduate program would be offered to hospital pharmacists, by Spease at Western Reserve University, and still another ten years before the second and third programs would be offered, at Baltimore and at Philadelphia.

Those who had the opportunity to receive their training under Mr. Whitney were enriched beyond measure. To his interns Mr. Whitney brought the inspirational qualities of kindness, patience, humility, generosity, courtesy, and sincerity which are the characteristics of a truly great teacher but ones to which students are too seldom exposed.

Mr. Whitney practiced what he preached. Under his guidance, the Pharmacy Department of the University Hospital became a *pharmacy service*. Members of the pharmacy staff, including interns, were well-indoctrinated with this concept of professional service. As a result of his teachings and precepts, his department at the University Hospital expanded from a small dispensary to an outstanding unit offering a comprehensive professional pharmaceutical service which has served as an inspiration to many. By building a truly great pharmacy service within his own hospital, Mr. Whitney gave his answer to those who believe pharmacy's salvation lies in slogans, "public relations," or other superficial measures. Mr. Whitney's service through knowledge was his public relations for pharmacy—and it is the only kind which will ever be lastingly effective.

During his lifetime Mr. Whitney participated in numerous activities for the advancement of pharmacy as a profession. He was responsible for the organiza-

tion of the Sub-Section on Hospital Pharmacy of the American Pharmaceutical Association, which developed into the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS in 1942. In 1943, Harvey Whitney joined with Leo Mossman of Gallipolis, Ohio to launch and edit the SOCIETY's first publication, the *Official Bulletin of the American Society of Hospital Pharmacists.* Mr. Whitney served as Vice President of the American Pharmaceutical Association in 1940-41. He also served as Chairman of the Section on Practical Pharmacy and Dispensing and Chairman of the Sub-Section on Hospital Pharmacy. Mr. Whitney was a member of the Revision Committee of the *National Formulary* from 1939 to 1944. He was the author of numerous articles pertaining to hospital pharmacy and related subjects. He was President of the Michigan Board of Pharmacy, President of the Michigan Branch of the American Pharmaceutical Association, and a member of Rho Chi.

Born in Adrian, Michigan, November 7, 1894, Mr. Whitney was graduated from Adrian High School in 1912. During the first World War he served in the Army and thereafter entered the College of Pharmacy of the University of Michigan where he received his Ph.C. degree in 1923. In 1925 he was appointed to the pharmacy staff of the University Hospital in Ann Arbor, and was named Chief Pharmacist in 1927.

To Harvey A. K. Whitney—teacher, student, hospital pharmacist par excellence, friend, leader—this first issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY is dedicated with gratitude for the devotion with which he served.

Harvey A. K. Whitney

has inspired all who practice in this specialty by his leadership and untiring efforts in bringing about a national organization for hospital pharmacists. As the first chairman of the American Society of Hospital Pharmacists, one of the first editors of THE BULLETIN *and a leader in establishing the internship programs, hospital pharmacists will always recognize his role in the advancement of their specialty during this era*

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as the president sees it—

LEO F. GODLEY, *Bronson Methodist Hospital, Kalamazoo, Michigan*

January, 1958. This is a memorable issue of THE AMERICAN JOURNAL OF HOSPITAL PHARMACY. It is the first time this name has appeared; and with this issue, this new title has gone all over the world. Beginning with this issue, hospital pharmacy is being represented by a monthly periodical and we are fortunate indeed.

This year is going to be a memorable one for the SOCIETY for other reasons too. We have a great deal of work and a lot of detail to accomplish by convention time in April. The Executive Committee met for a day and a half in Washington just prior to the Pan-American Congress in November. We are continuing with a meeting here in Kalamazoo the 24th and 25th of this month. We are hoping that we can get all the work done in two days.

Secretary Gloria Francke tells me that reports from the special committees are coming in already. We are going to discuss this work in detail. This year, we have a special committee working with a standing committee. The Special Projects Committee has been cooperating with the Committee on Minimum Standards. Mr. Teplitsky has corresponded with the affiliated chapters encouraging group consideration of the Minimum Standards. Through an "all out" effort in this important area, we would hope to contribute to the effectiveness of the Minimum Standards Committee. The importance of a standard of practice cannot be over emphasized

As yet we have had no liaison activity with the national nursing organizations. We are hoping that we can establish an effective connection through our special committee activity on Safety Practices and Procedures. There has been much discussion recently about medication errors on the nursing floors. It is possible that we can build a beneficial relationship with nursing organizations in this important area. If we can work out some effective guide lines in this regard, the American Hospital Association has indicated that such material could be included in the manual on hospital pharmacy which is being prepared by their Council on Professional Practice.

Robert Lantos is chairman of the Committee on Safety Practices and Procedures. He has been busy collecting background material on medication errors and accidents. He has sent out blank report forms to collect statistical information. It may be that he will want to modify his questionnaire; but this will have to be decided from the material he collects in the first sample. He needs our cooperation; please send him your ideas and suggestions.

In a chat with Joe Oddis a few days ago, he told me he was working on the arrangements to determine the places where the 1959 Institutes are to be held. Salt Lake City seems to be first choice. Mr. Oddis wants to make location arrangements for at least two years in advance. The 1958 locations are Chicago and Philadelphia.

The 1958 Institute programs are beginning to take shape. I'd certainly like to hear from you if you have ideas on what the Institute programs should include. A good file on program suggestions is a thing we should begin to build. Program Chairman Walter Frazier has a first rate schedule of topics planned for us in Los Angeles.

Last August, in Chicago, Dr. Kenneth Babcock, Director of the Joint Commission on Accreditation of Hospitals, participated in a panel discussion on the formulary system. His views were most favorable and interesting. In the December 1957 issue of the *Bulletin of the Joint Commission* he has devoted considerable discussion to the pharmacy and the formulary system. It would be a good idea for us to read it and discuss it with our associates, particularly our administrators and the members of our pharmacy committees.

January 1958. The President's office will begin the calendar year with some engagements already scheduled for the month: a meeting with the Michigan Society, a two day meeting of the Executive Committee in Kalamazoo, and a one day meeting of the Joint Committee of the ASHP and AHA in Washington.

Happy New Year!

LEO F. GODLEY

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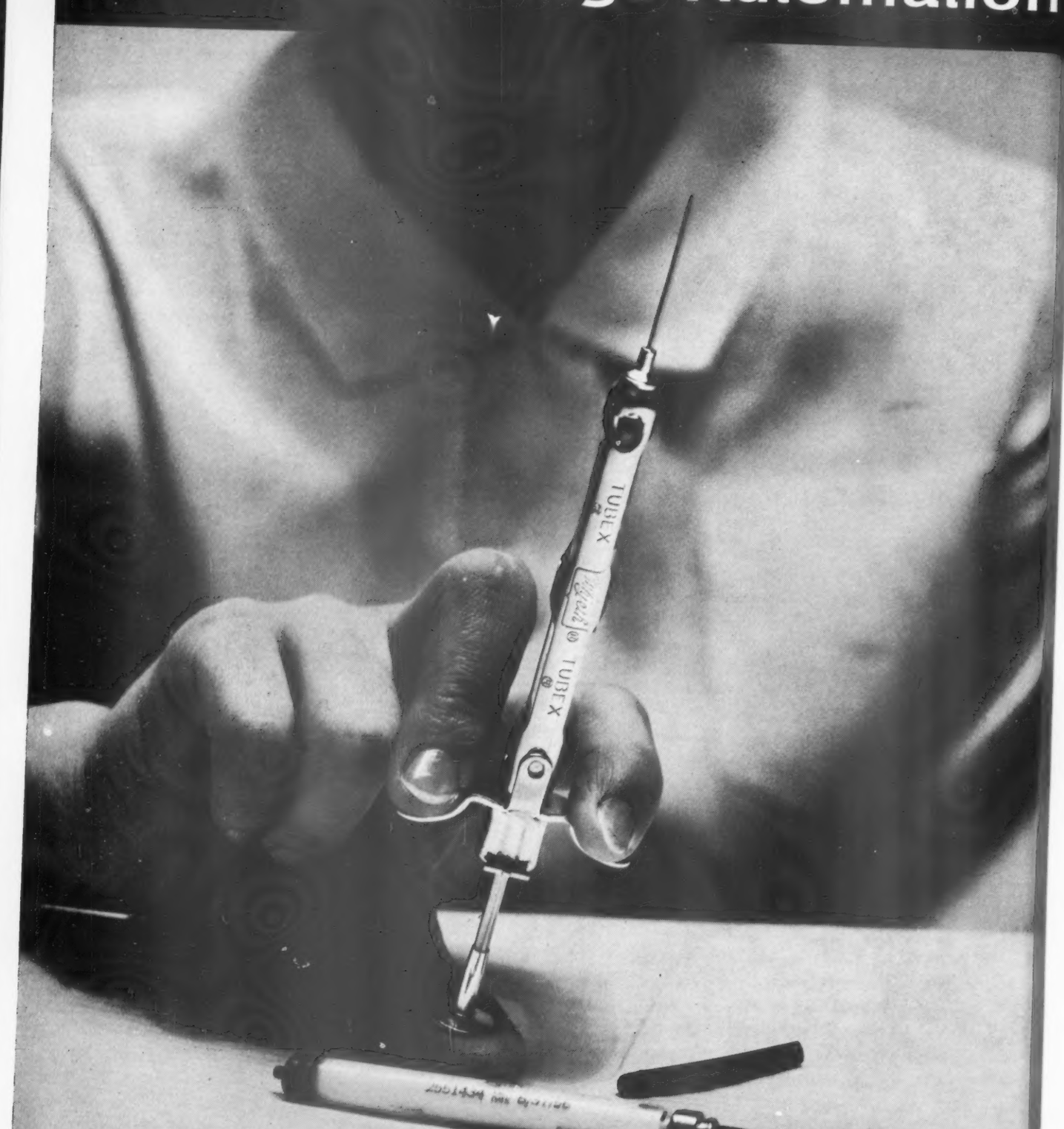

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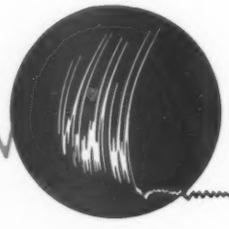
1. Jones, Georgeanna S. and Smith, Frank: Am. J. Obstet. Gynecol., Vol. 67: No. 3, 628-633, 1954.

2. Majewski, J. T. and Jennings, T.: Obstetrics & Gynecology, Vol. 5, No. 5, 1955.

3. Majewski, J. T. and Jennings, T.: Obstetrics & Gynecology, Vol. 9, No. 3, 1957.



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Midwest Sisters' Association

Members of the Midwest Association of Sister Pharmacists met for their tenth anniversary meeting at St. Mary's Mercy Hospital, Gary, Indiana on September 19. The principal speakers included Reverend James Moscow, Assistant Director of Hospitals for the Archdiocese of Chicago and Mr. Joseph Oddis, Staff Representative of the Council on Professional Practice of the American Hospital Association. Included also on the program was a brief history of the Midwest Association by Sister M. Tarcissa.

The November 21 meeting of the Midwest Association of Sister Pharmacists was held at St. Francis Hospital in Blue Island, Illinois. Following announcements, including participation of affiliated chapters in the revision of the Minimum Standards for Pharmacies in Hospitals, suggestions for the 1958 H.A.K. Whitney Award, the C.H.A. Pharmacy Institute, and the two week pharmacy workshop which is to be sponsored also by the C.H.A., the members heard a panel discussion on "The Dangers of Cortisone (Steroids) Therapy." Participants included Mr. Robert Turley of Merck Sharp and Dohme; Mr. Alfred Fleishman of Schering Corporation; and Mr. Albert Weissman of Organon. Emphasis was placed on the dangers involved and the undesirable reactions to such therapy, particularly when used over a period of time.

Members attending the meeting also had an opportunity to examine several interesting features in the Pharmacy Department. Sister Tarcissa, Chief Pharmacist, explained the operation of a narcotic alarm system, a prescription file drawer set, and the ever useful drug elevator.

The February meeting of the Midwest group will be held at St. Bernard's Hospital in Chicago with President Sister Anne Gallagher serving as hostess.

Texas Society

The Texas Society of Hospital Pharmacists will have two business meetings at the time of the Tenth Annual Hospital Pharmacy Seminar which will be held at the University of Texas College of Pharmacy February 14 to 16. The first business meeting will be held at 8 P.M. on Friday, February 14, at the Austin Hotel. An Executive Council meeting is scheduled at 7 P.M. just prior to the regular meeting on Friday evening. The next business meeting of the Society will be at 8 A.M. on Sunday, February 16, at the College of Pharmacy Building.

Members of the Program Committee of the T.S.H.P. who have worked with Mr. Joe Arnette, Director of the Extension Division of the College of Pharmacy are Robert Lantos, University of Texas Medical Center, Galveston; James McKinley, M.D. Anderson Hospital, Houston; and Susan Campbell, Baptist Memorial Hospital, Beaumont.

Dade County Society of Hospital Pharmacists

The Dade County Society of Hospital Pharmacists postponed their November meeting due to the sudden death of their Vice-president, Mr. Max Kanter.

The December meeting held at the home of the Treasurer, Mrs. Rena Finegan, on December 10, 1957. The Miami Branch of the American Pharmaceutical Association joined the group for this meeting.

Philadelphia Hospital Pharmacists Association

The regular meeting of the Philadelphia Hospital Pharmacists Association was held at the U. S. Naval Hospital on October 15. Fifty-five members and guests were present. President Herbert Flack introduced Lt. William Kolb, Pharmacist in Charge, who welcomed the group and discussed briefly the size of the hospital together with the functions and purchasing methods in a military institution.

The topic of the Program for the evening was "Packaging and Labeling Concepts." Many members exhibited and described pieces of equipment which they have found helpful as well as labor saving in the hospital pharmacy department.

"Accidental Poisoning in Children," was the subject of a paper by Mr. Joseph D'Ambola presented at the September 17 meeting of the Philadelphia Hospital Pharmacists Association. The meeting was held at the Jefferson Medical College Hospital.

Greater St. Louis Hospital Pharmacists

Members of the Hospital Pharmacists Association of Greater St. Louis met at the St. Louis College of Pharmacy and Allied Sciences on Tuesday, October 8. Reports were made on the work of the Membership Committee and the efforts to get members out to meetings. On the recommendation of Vice-President Joseph Guller, the group voted to join with the St. Louis Council, a new organization representing all segments of Pharmacy. Mrs. Florence Mueller and Mr. A. J. Dellande were appointed to serve as liaison officers with the Council.

Cleveland Society

Members of the Cleveland Society of Hospital Pharmacists met at the Welfare Federation Building in Cleveland on December 4. The Program, under the title "Creative Thinking in Business," was in the charge of Mr. William O. Uraneck of the Ford Motor Company. A schedule of the program for the evening was opened by Mr. Paul Magalian of Crile Veterans Hospital in Cleveland. The introduction included a discussion of "Need for Creativity in Business," and "History of the Deliberative Thinking Movement." Under Brainstorming Technique, four rules were pointed out—(1) no judicial thinking; (2) quantity breeds quality; (3) the wilder the idea the better; and (4) combination ideas acceptable. This was followed by a panel demonstration on selected problems from the field of pharmacy.

Greater Kansas City Society

Fifteen members of the Society of Hospital Pharmacists of Greater Kansas City met at the Blue Cross-Blue Shield Building on October 9 at 2 P.M. Business included suggested changes in the Constitution and By-Laws, the proposed revision of the Minimum Standard for Pharmacies in Hospitals with the suggestion that affiliated chapters make an effort to re-evaluate the Standard, and a proposal for a progressive educational pharmacy program.

Members of the group were invited to attend a radiological monitoring course which will be given at Kansas City University in the spring. This is a Civil Defense Program sponsored by the state of Missouri.

Southeastern New York State Chapter

Members of the Southeastern New York State Chapter of the ASHP met at the Lenox Hill Hospital in New York City on November 14 with President Harold Neham presiding. During the business session, Mr. Neham, who served as the delegate to the ASHP Annual Meeting, reported on the Convention and ASHP activities in general.

Mr. Robert Bogash, President Elect of the ASHP, spoke on activities in the national organization and plans for the future.

Greater New York Chapter

On November 19, the Greater New York Chapter of the American Society of Hospital Pharmacists met at St. Vincent's Hospital, Staten Island. Sister M. Virginia, President, presided.

Sister Etheldreda acquainted the group with the latest developments of the anticipated one-day Pharmacy Seminar which is planned for early January and is expected to include Sister Pharmacists from neighboring states. Thus, it will assume a regional aspect.

The workshop planned by the Catholic Hospital Association was briefly outlined. Sister Etheldreda also brought the group up to date on the Institute to be held in Atlantic City next June.

The special topic for this meeting included an exhaustive group study of the excellent article, "The Law of Hospital Pharmacy," by Dr. George Archambault.

Guests of the chapter on this occasion were the Sister students of St. John's and Fordham's Colleges of Pharmacy. They shared the interest and enthusiasm of the members in this masterpiece of Dr. Archambault's and agreed that he is to be congratulated on his untiring efforts to aid his fellow pharmacists.

Colorado Society

Members of the Colorado Society of Hospital Pharmacists met on October 15 at the St. Anthony Hospital in Denver. The principal item of business was concerned with the Constitution and By-Laws. The group has recently applied for affiliation with the national organizatcn and will submit its constitution for approval.

The program included a discussion on "Responsibility of Organized Pharmacy," by Mr. Verne N. Seeley, editor and publisher of the *Rocky Mountain Druggist*.

Oklahoma Society

Mr. Al Mannino, Director of the Hospital Pharmacy Division of McKesson and Robbins, Inc. of New York, was the principal speaker at the November 14 meeting of the Oklahoma Society of Hospital Pharmacists. Members of the group were guests for a noon luncheon held at the Oklahoma City Branch of McKesson and Robbins. Mr. Mannino was introduced by Mr. Dan M. Donaldson, Division Manager. On speaking on "The Future of Hospital Pharmacy," Mr. Mannino emphasized the pharmacist's responsibility to the patient and the allied professions.

Following the program, new officers for the coming year were installed including *President,* Ralph E. Reed, Student Health Center of the Oklahoma University College of Pharmacy, Norman; *Vice-President,* David L. McLemore, formerly Pharmacist at Mercy Hospital, Oklahoma City; and *Secretary-Treasurer,* Sister M. Teresa, St. Anthony Hospital, Oklahoma City.

Following the meeting, members had an opportunity to tour the plant of McKesson and Robbins and were acquainted with the operation and services rendered.

Oklahoma Society—Left to right: Ralph Reed, Incoming President; A. A. Maninno, McKesson Robbins, Inc.; and Sister Mary Teresa, Outgoing President

A highlight in recent meetings of the Oklahoma Society was the first one-day Seminar which was made possible through the courtesy of the Pfizer Laboratories and was held at the Lockett Hotel in Norman on September 28. With 76 hospital pharmacists participating, the national organization was represented by President Leo F. Godley who extended greetings on behalf of the ASHP and spoke on "The Road Ahead for Hospital Pharmacy."

Another feature of the program was a presentation on "Effective Communications for Hospital Pharmacists," by Mr. E. Burns Geiger of Pfizer Laboratories. Other subjects covered during the Seminar included drug control and distribution in hospitals, new advances in drug therapy, teaching responsibilities of the hospital pharmacist, the pharmacist's responsibility as Secretary of the Therapeutics Committee, the hospital pharmacist and the medical profession, and potential sources of errors in the administration of medicine. The program also included a hospital pharmacy forum with representatives from various segments of pharmacy participating.

Massachusetts Society

"Accidental Poisoning in Children," was the principal subject covered at the September 18 meeting of the Massachusetts Society of Hospital Pharmacists. The speaker, Dr. Robert J. Haggerty, is Executive Secretary of the Boston Poison Information Center and Assistant Physician of the Child Health Division of the Children's Medical Center. The meeting was held at the Children's Medical Center.

During the business session announcements were made regarding future meetings and subjects for consideration. These included pricing, prepackaging, and manufacturing solutions.

Northeastern New York Society

The regular monthly meeting of the Northeastern New York Society of Hospital Pharmacists was held on Wednesday, October 30, at the Ellis Hospital, Schenectady, New York. After dinner, Dr. George W. Graham, Director, spoke of the building program now in progress at Ellis Hospital. The meeting was attended by 39 members and guests. Following the program, a business meeting was conducted. This included the reports of the various committee chairmen and plans were outlined for the forthcoming year. The group was requested to nominate a hospital pharmacist for the Harvey A. K. Whitney Award. This was carried out. Of particular note, at the meeting was that we had recruited 23 new members of the chapter, including five students and three national members.

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COMPLETED PROJECTS

ASHP Affiliated Chapters

BENJAMIN TEPLITSKY, *Chairman,* Committee on Special Projects

Listed below are ten completed projects conducted by various Chapters of the American Society of Hospital Pharmacists. A brief description of the projects, as well as individuals to contact for additional information is included

Hospital Pharmacy Survey

Washington State Hospital Pharmacists

An extensive detailed survey dealing with prescription pricing, inventory, figures, routine operational methods and formularies is presented. This survey contains many and varied statistics which are interesting.

Contact **Joseph E. Birmingham or Elmer M. Plein, University of Washington, Seattle, Washington.**

History of Houston Area Society of Hospital Pharmacists

Houston Area Society of Hospital Pharmacists

A complete historical record of the Houston Chapter is presented since its formation in 1946. A chronological list of activities and a present day membership list are included.

Contact **Miss Adela Schneider or Dr. Ruth Kroeger, Southern Pacific Hospital, Houston, Texas.**

The Pharmacy Phase of Hospital Disaster Plan

Western Pennsylvania Society of Hospital Pharmacists

A comprehensive outline is presented concerning the duties of the pharmacy staff members in a state of emergency. Also, a list of emergency drugs is presented and a source of supply list.

Contact **C. B. Cleveland or Sister Mary Gonzales, Mercy Hospital, Pittsburgh 18, Pennsylvania.**

Approach of Drug Manufacturers to List Information On New Drugs on 3 x 5 Cards for Uniform Filing

Western Pennsylvania Society of Hospital Pharmacists

A sample format of a 3 x 5 Literature Index Card is submitted to the National Pharmaceutical Council in order to standardize Literature Index Cards of all pharmaceutical manufacturers.

Contact **I. Bianculli, Pharmacy Service, VA Hospital, Leech Farm Road, Pittsburgh 6, Pennsylvania.**

A Study of Costs of Hospital Manufactured Sterile Solutions at Akron City Hospital

Akron Area Society of Hospital Pharmacists

A statistical report is presented concerning the cost of maintaining a manufacturing program on sterile solutions at Akron City Hospital. This includes a cost and volume analysis.

Contact **R. F. Lovell, R. P., The City Hospital of Akron, Akron 5, Ohio.**

Houston Area Hospitals and Pharmacists—a Pictorial Survey

Houston Area Society of Hospital Pharmacists

This special project presents a brief history and description of the hospital and its pharmacy with pictures. Certainly one of the most elaborate special projects ever completed. An excellent piece of work which bears review.

Contact **Adela Schneider, Southern Pacific Hospital, Houston, Texas; or W. W. Murray, Methodist Hospital, Houston Texas; or Dorothea Siler, St. Luke's Hospital, Houston, Texas.**

Visitation Program

Akron Area Society of Hospital Pharmacists

An outline and schedule of a two-day visit of selected pharmacy students from four colleges of pharmacy to three hospitals in the Akron Area. This visitation project is conducted by the Hospital Pharmacists' Society and it is a regular chapter meeting.

Contact **John D. Smittle, President, Akron Area Society of Hospital Pharmacists.**

Seminar on Sterile Solutions

Rochester Area Society of Hospital Pharmacists

A series of four lectures encompassing various phases of parenteral solutions including history, equipment, techniques involved. A must reading for pharmacies contemplating the introduction of self manufactured parenterals.

Contact **William Whitcomb, Rochester General Hospital, Rochester 21, New York.**

Accidental Poisonings

Northeastern N. Y. Society of Hospital Pharmacists

A survey of 13 hospitals in New York, Massachusetts and Vermont representing over 4,000 beds showed that almost 75% of all accidental poisionings in a six month period occurred in children under 4 years of age.

Contact **William Hotaling, Ellis Hospital, Schenectady, New York.**

Pharmacist Positions in Neighboring States and Indiana

Indiana Society of Hospital Pharmacists

A survey of pharmacists in state hospitals which includes such things as salary range, job descriptions, and miscellaneous services, is presented in detail. A survey which may be worthwhile to a person setting up a large pharmacy with work responsibility.

Contact **A. L. Larrison, Consulting Pharmacist, Department of Health, 1330 W. Michigan Street, Indianapolis, Indiana.**

in the hospital the diuretic must work

If the first diuretic used in the patient hospitalized for heart failure is ineffective, it may be too late to try another. For this reason and many others, physicians prefer the dependability of injected MERCUHYDRIN.®

Experience with innumerable patients in several decades of use confirms the uniformly rapid response to MERCUHYDRIN with a minimum of side effects. This assured action saves lives, saves time, saves money. And when recovery is well underway, switching to oral NEOHYDRIN® has the further advantages of saving injections for the patient and time for your nursing staff.

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A STANDARD FOR INITIAL CONTROL OF SEVERE FAILURE

MERCUHYDRIN®

BRAND OF MERALLURIDE INJECTION SODIUM

FOR MAINTENANCE OF THE EDEMA-FREE STATE

NEOHYDRIN®

BRAND OF CHLORMERODRIN TABLET

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Now everybody's talking...

about... *closer control of cross infection in every part of the hospital*

Wider recognition of the current problem of hospital-acquired infections is focusing new attention on ways and means of reducing this hazard to good patient care. Hospital and medical society meetings—and hospital, medical and surgical journals—are daily shedding new light on the varied aspects of the overall problem.

In many hospitals, a special "committee on cross infection" has been appointed to review practices and procedures. In others, each department head is studying closely his or her own methods of operation. Few hospitals exist which are not giving some special thought to this highly current problem.

Out of this critical evaluation has grown an awareness that environmental asepsis is a major weapon for cutting cross infection to a minimum. Application of continuous disinfection procedures from operating rooms through food service and laundry areas can be the means to changing the hospital's entire experience with hospital-acquired respiratory, intestinal, urinary or post-operative wound infections.

Take floors, for instance

Floors offer a great opportunity for furthering the spread of infection. Microorganisms settling to the floor are redispersed on dust particles or tracked through the hospital on shoes. Walls and ceilings as well can be reservoirs of potential infection. Lehn & Fink disinfectants not only kill all the most common pathogens on contact but are continuously active against new contaminants touching the disinfected surface for as long as a week later.

While the patient is there

Concurrent disinfection is practical whether or not the patient is "isolated." Wiping of furniture and fixtures and damp mopping of floor, with a disinfectant, stop air- and floor-borne microbes at the source.

In the operating room

Lehn & Fink disinfectants have many applications here. Among them: mopping floors; cleaning grills, ducts, and coils of air conditioners; as standard equipment on the scrub-up cart; as a germicidal dip to remove gross contamination from gloves before their removal; to gather instruments into enroute to sterilizer.

Other L & F disinfectant applications are many: for disinfection of instruments with lens systems, to wipe and store thermometers, to sanitize utensils, etc. In all instances, action is bactericidal, fungicidal and tuberculocidal.

Which L & F disinfectant?

Lysol®, O-syl® and Amphyl® do the same disinfecting job. Any one of them kills bacteria, fungi, and TB bacilli efficiently, but each has individual characteristics.

Lysol was far ahead of its time when introduced over sixty years ago. Recently the formula was improved; the odor was lightened and toxicity was reduced so that the "poison" label is no longer needed. Many hospitals prefer Lysol because of its long reputation for dependability. The characteristic odor is preferred by many for psychological reasons or as an indication that disinfection with Lysol has just been done.

O-syl is preferred by hospitals wanting all the germicidal efficiency of Lysol but without the odor. It is practically odorless when diluted for use. Like Lysol, O-syl is highly concentrated. Only a 1% solution of either (1 part to 100 of water) is needed for most applications.

Amphyl is also odorless when diluted for use. Convenience and low cost due to its high concentration often make Amphyl the disinfectant of choice. Amphyl is twice as powerful as Lysol or O-syl but does not cost twice as much. A ½% solution (1 part in 200 of water) is sufficient for general disinfection so that the cost per gallon of "use dilution" is less than with Lysol or O-syl. When expected contamination is great, as in TB or isolation wards, Amphyl is often preferred.

Let's talk about it

Solving the problem of environmental infection has been the business of Lehn & Fink since 1874. Solving such problems arising in your own hospital usually takes more than talk—but perhaps you would like to discuss them with our technical specialists. We can function as a part of your "committee on control of cross infection," perhaps suggest procedures, and supply informational material for teaching purposes. At any rate, please ask us. Specially trained field service representatives as well as the technical staffs in our New York office and in our laboratories at Bloomfield, New Jersey, are available for consultation.

• • •

Lehn & Fink disinfectants are available through your surgical supply dealer.

If you want literature, samples, or assistance in setting up procedures, please write:

Lehn & Fink *Professional*
PRODUCTS CORPORATION DIVISION
445 PARK AVENUE, NEW YORK 22, N.Y.

SPECIALISTS IN ENVIRONMENTAL ASEPSIS
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News

Fischelis To PHS Committee

Dr. Robert P. Fischelis, Secretary of the American Pharmaceutical Association, has been named to the Advisory Committee on the U. S. National Health Survey. The Committee, according to Dr. Leroy E. Burney, Surgeon General, U. S. Public Health Service, will review plans and progress of the Health Survey and assist in formulating principles and methods of cooperation with interested private and public organizations. Membership on the Committee includes representatives of health professions, insurance organizations, safety interests, labor industry and other users of health statistics.

Anna Richards Honored

Anna C. Richards

Mrs. Anna Cona Richards, Chief Pharmacist at Mountainside Hospital, Montclair, N. J., was recently the recipient of the Orange (N.J.) Unico "Outstanding Citizenship" Award. Mrs. Richards, well known to hospital pharmacists throughout the country, has served as President and Vice-President of the New Jersey Society of Hospital Pharmacists. In the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, she has served on numerous committees and participated in national activities, including attendance at the 1953 Congress of the International Pharmaceutical Federation in Paris and the Pan-American Congress of Pharmacy and Biochemistry in Sao Paulo in 1954.

Mrs. Richards is a summa cum laude graduate of the Rutgers School of Pharmacy in Trenton, N. J. In 1953 she received an honorary membership in Rho Chi at Rutgers. She has served on the Rutgers Conference Committee for six years and, as Chairman of the Evaluation and Interprofessional Committee, she helped establish the course in Hospital Pharmacy Administration.

CHA Receives Educational Grant

Saint Louis University and the Catholic Hospital Association have received a $100,000 grant for projection of the C.H.A.'s department of continuing education through the medium of formal classes for hospital department heads and supervisory personnel. Formal classes are scheduled to include all hospital areas, professional and service, are designed to present the latest developments and teach new techniques applicable to any given area. This program, first of its kind in the field, bases its curriculum development upon the assumption that at the end of three to five years, a further period of study will be offered.

Heading the Catholic Hospital Association's department of continuing education is Mr. John T. James who holds a Master's degree in hospital administration from Northwestern University. He also has served as administrator of Park Avenue Hospital Rochester, N. Y., and is at present an instructor in hospital administration at St. Louis University.

►*Dr. H. A. B. Dunning* was honored on his eightieth birthday by the Maryland Pharmaceutical Association. Speakers at the dinner in Baltimore on October 24 included Dr. Robert L. Swain, Dr. W. Paul Briggs, and Dr. Robert P. Fischelis.

Historical Photographs Wanted

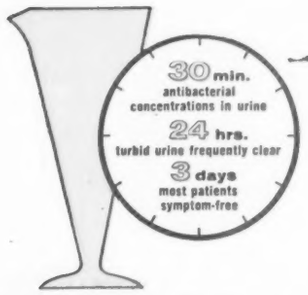
The American Institute of the History of Pharmacy has appealed for "historical photographs of pharmacy in action." In making the appeal, Dr. Glenn Sonnedecker, Director of the Institute, urges every pharmacist "to find out what is in his files, or perhaps in a basement box or attic trunk, that should be publicly preserved to help future generations of pharmacists understand their professional heritage and their predecessors." In this new effort, the Institute is following up a suggestion made earlier in the year by George Bender of Detroit, current president of the A.I.H.P., who called for more systematic efforts to get irreplaceable historical material safety into the Institute's reference collections.

Hospital pharmacists having access to historical photographs, as well as documents, may direct them to the American Institute of the History of Pharmacy, School of Pharmacy, Madison 6, Wisconsin.

►*This Month in Washington* is the title of a new monthly report available from the Washington Service Bureau of the American Hospital Association. The report, which is sent to all members of the Association, is a means of keeping hospital people informed regarding activities affecting the health professions. "This Month in Washington" is prepared by Mr. Kenneth Williamson, Associate Director of the Association and Director of the Washington Service Bureau.

in urinary tract infections of pregnancy delay is dangerous...

"Approximately one-half of the patients have some permanent damage to the urinary tract."[1]



FURADANTIN® *first...*

BRAND OF NITROFURANTOIN

FOR RAPID ERADICATION OF INFECTION

Specific for genitourinary tract infections • rapid bactericidal action against a wide range of gram-positive and gram-negative pathogens and organisms resistant to other agents • negligible development of bacterial resistance • excellent tolerance —nontoxic to kidneys, liver and blood-forming organs • safe for use in pregnancy[2,3]

AVERAGE FURADANTIN DOSAGE: 100 mg. q.i.d. with food or milk. Continue treatment for 3 days after urine becomes sterile.

SUPPLIED: Tablets, 50 and 100 mg. Oral Suspension (25 mg. per 5 cc. tsp.).

REFERENCES: 1. Rives, H. F.: Texas J. M. **52**:224, 1956. 2. Diggs, E. S.; Prevost, E. C., and Valderas, J. G.: Am. J. Obst. **71**:399, 1956. 3. MacLeod, P. F., et al.: Internat. Rec. Med. **169**:561, 1956.

NITROFURANS

a new class of antimicrobials—neither antibiotics nor sulfonamides

EATON LABORATORIES NORWICH, NEW YORK

Hospital Pharmacist on Television

Edward W. Tighe

Edward W. Tighe, Pharmacist-In-Chief, General Hospital, Lancaster, Pa., and a member of the ASHP, was recently featured on a program dealing with medical science televised over WCAL-TV. Called "Conquest of Disease," the program highlighted some of the great medical discoveries that have more than doubled man's life within the past several hundred years, and brought out the importance of the physician-pharmacist team in guarding the nation's health. The program utilized a script, visual aids, and a short film clip made available by Lederle Laboratories Division, American Cyanamid Company.

►*John J. Zugich,* a past president of the ASHP, participated in the Hospital Pharmacists' Section of the Ontario Hospital Association Convention, in Toronto on October 29. Mr. Zugich, formerly a practicing hospital pharmacist, is an Assistant Administrator at University Hospital, Ann Arbor, Mich. He holds a Bachelor's Degree in Pharmacy and a Master's Degree in Public Health.

►*Allen V. R. Beck,* Chief Pharmacist at Indiana University Medical Center, Indianapolis, Ind., was the official delegate from the ASHP to the A.Ph.A. House of Delegates meeting in Washington, D. C., November 10 and 11.

New Publication Issued

"Current Contents of Pharmaceutical Publications," is the title of a new publication designed to make available to researchers, administrators, field representatives, and clinicians the contents pages from periodicals. Organizations subscribing to Current Contents service receive multiple copies of a weekly pocket-size booklet containing photographic reproductions of the current or advance table of contents of nearly 250 periodicals. For a list of the journals covered, specimen copies, and any additional information, write to: Eugene Garfield Associates, 1523 Spring Garden St., Philadelphia 30, Pa.

AHA—ASHP Joint Committee Members

Mr. C. P. Cardwell, Jr., Medical College of Virginia, Hospital Division, Richmond, has been named as one of the American Hospital Association's representatives to the Joint Committe of the A.H.A. and ASPH. Other A.H.A. members include Dr. Robert Cadmus, North Carolina Memorial Hospital, Chapel Hill, Chapel Hill, N. C.; C. Joseph Vance, Blue Cross-Blue Shield of Alabama, Birmingham, Ala.; and John J. Zugich, University Hospital, Ann Arbor, Mich.

ASHP representatives on the Joint Committee are George F. Archambault, U. S. Public Health Service, Washington, D. C.; Don E. Francke, University Hospital, Ann Arbor, Mich.; Walter M. Frazier, Springfield City Hospital, Springfield, Ohio; and Evlyn Gray Scott, St. Luke's Hospital, Cleveland, Ohio. President Leo F. Godley and Secretary Gloria Francke are *ex-officio* members of the Committee.

Joseph Oddis, Staff Representative of the A.H.A.'s Council on Professional Practice and Paul Parker, Director of the Division of Hospital Pharmacy of the A.Ph.A. and ASHP, are also *ex-officio* members of the Committee.

►*The American Society of Hospital Pharmacists'* Executive Committee met in Washington, D. C. on November 2 and 3. The meeting was held in conjunction with the Pan-American Congress of Pharmacy and Biochemistry which was held at the Mayflower Hotel in Washington, November 3-9. Actions taken by the Executive Committee will be reported in the February issue of the JOURNAL.

►*Members of the ASHP Executive Committee,* as well as other hospital pharmacists, participated in the Fourth Pan-American Congress of Pharmacy and Biochemistry held in Washington, November 3-9.

Lunsford-Richardson Awards

The Lunsford Richardson Awards—sponsored by Vick Chemical Company and its two pharmaceutical subsidiaries, The Wm. S. Merrell Company and The National Drug Company—have been announced. Designed to encourage students to investigate current pharmacy problems, to summarize and present their findings for the benefit of other students and investigators, and to broaden student interest in the profession of pharmacy, awards will be presented to undergraduate and graduate students and the Schools of Pharmacy attended by the winning students. For additional information, contact Dr. M. A. Chambers, Professional Service Manager, The Wm. S. Merrell Company, Cincinnati 15, Ohio.

►*John Selak,* who has been a member of the pharmacy staff at the University of Chicago Clinics since 1954, returned to his native city, Reading, Pennsylvania, December 1st, because of the death of his father.

Recipients of Lederle Research Grants

Recipients of research grants made available to the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS through Lederle Laboratories are: Alex Berman, University of Michigan College of Pharmacy, Ann Arbor, Mich.; John W. Webb, Massachussetts General Hospital, Boston, Mass.; Calvin D. Gilliam, Veterans Administration Center, Los Angeles, Calif.; Donald M. Friedman, Veterans Administration Center, Los Angeles, Calif.; James Eleiff, Veterans Administration Center, Los Angeles, Cali.; William M. Heller, University of Arkansas Medical Center, Little Rock, Ark.; Paul F. Parker, Division of Hospital Pharmacy of the American Pharmaceutical Association and AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, Washington 7, D. C.; and Charles M. King and Herbert L. Flack, Jefferson Medical College Hospital, Philadelphia, Pa.

Funds from the grant made through the SOCIETY are allocated for research for the improvement of hospital pharmacy services and for the formulation and development of pharmaceuticals prepared in hospital pharmacies.

Reviews of the requests for grants are made by a Selection Board which includes, Dean Glenn Jenkins of the Purdue University School of Pharmacy, Lafayette, Ind.; Dr. Don Skauen of the University of Connecticut School of Pharmacy, Storrs, Conn.; and Dr. W. Arthur Purdum of The Johns Hopkins Hospital and University of Maryland School of Pharmacy, Baltimore, Md. Mr. Paul Parker, Director of the Division of Hospital Pharmacy serves as Secretary of the Committee. The actions of the Selection Board are finally submitted to the ASHP Executive Committee for approval.

Administration of the program, including screening of projects to be submitted to the Selection Board for consideration, is under the direction of the Committee on Research and Development headed by Milton W. Skolaut, Chief, Pharmaceutical Service, Clinical Center, National Institutes of Health, Bethesda, Md. Other members of the Committee who serve for three year terms on a rotating basis include Dr. William Heller of the University of Arkansas Medical Center, Little Rock, Ark.; and Mr. Charles Towne of the Veterans Administration Center Los Angeles, Calif.

►*The American Chemical Society's* Division of Medical Chemistry will meet in San Francisco, April 13-18. Included on the program will be a symposium on "Newer Synthetic Methods in Medical Chemistry."

►*Ciba Pharmaceutical Products, Inc.* dedicated new pharmacy research and development laboratories in Summit, N. J. on November 21. Ceremonies dedicating the new building were part of a two-day program including guided tours. Jack Cooper, Director of Pharmacy Research and Development Division, heads the laboratories.

►*Dr. Edward A. Brecht,* Dean of the School of Pharmacy at the University of North Carolina, has recently been elected President of Rho Chi, national pharmacy honor Society.

►*The American College of Apothecaries* held its Mid-Year Conference in St. Louis, Mo., October 20 through 22.

Webster Dean at Illinois

George L. Webster

Appointment of Dr. George L. Webster as Dean of the College of Pharmacy of the University of Illinois has recently been approved by the University Board of Trustees on the recommendation of President David D. Henry. Dr. Webster, 57, is a national authority on pharmaceutical education. He is Professor and Head of the Chemistry Department at the College of Pharmacy and will continue these duties until a successor is chosen. Effective Jan. 1, 1958, Dr. Webster succeeded Dean Earl R. Serles, who headed the college for 17 years until his death on March 13, 1957. The college is housed in a $6,500,000 classroom and laboratory structure at 833 S. Wood St., Chicago.

Dr. Joseph S. Begando, Associate Dean, has been in charge of the college since Dr. Serles' death. He will continue as Assistant Dean and Associate Professor of Pharmacy Administration.

Appointment of Dr. Webster was praised by Dr. Herbert E. Longenecker, Vice President in charge of the Chicago Professional Colleges.

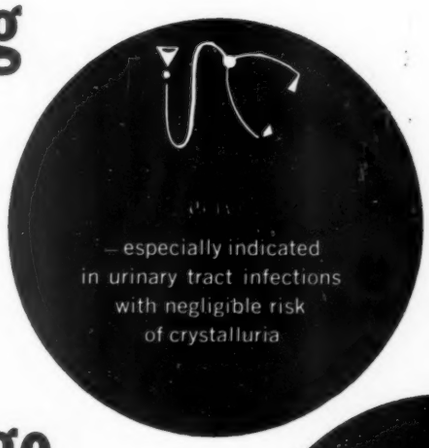
"Dr. Webster brings to the deanship the knowledge and experience of a long and distinguished career as a teacher, departmental administrator, participant in university-wide educational policy groups, and national leader in pharmaceutical education," Dr. Longenecker said. "His fine personal qualities, coupled with his wide experience, place him at the top in the esteem of his colleagues."

Dr. Webster joined the staff of the College of Pharmacy in 1922 and was elevated through various

Everybody benefits from this new, long-acting sulfa that cuts dosage over 75%

—reduces inventory... simplifies stock control and handling

—a real space-saver... 1 tablet a day does the work of 8 other sulfa tablets



—especially indicated in urinary tract infections with negligible risk of crystalluria

—greater acceptability... unbroken sleep

—a time and step-saver... a single maintenance dose provides 24 hours antibacterial activity

Tablets: Each quarter-scored, peach-colored tablet contains 0.5 Gm. (7½ grains) of sulfamethoxypyridazine. Bottles of 24, 100 and 1000 tablets.

Syrup: Each teaspoonful (5 cc.) of caramel-flavored syrup contains 250 mg. of sulfamethoxypyridazine. Bottles of 4 fl. oz.

SULFAMETHOXYPYRIDAZINE LEDERLE

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LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

Lederle

faculty ranks to Professor in 1941. He became Chairman of the Chemistry Department in 1947.

Dr. Webster is Secretary-Treasurer of the American Association of Colleges of Pharmacy, and Grand Counselor of Kappa Psi Pharmaceutical Fraternity. He is a Past President of the Association of Vitamin Chemists, and Rho Chi, national honor society in pharmacy.

He also has been Director of the American Foundation for Pharmaceutical Education; member, executive committee of the American Association of Colleges of Pharmacy; and member of the U.S. Pharmacopeia Commission on Revision.

Within the university he is chairman of the 3-campus Senate Coordinating Council; chairman, Committee on Educational Policy, Chicago Professional Colleges Senate Committee; and member of the University Committee on A Four Year Program for the Chicago Undergraduate Division. He is the author of numerous scientific articles. His research interests include organic arsenicals, local anesthetics, alkaloidal assays, and vitamin assays.

Dr. Webster was born in Maquoketa, Iowa, on Nov. 30, 1900. He received his Ph.G. degree from the University of Illinois in 1922. At the University of Michigan he was awarded a B.S. in 1927, M.S. in 1931, and Ph.D. in 1937. Dr. Webster and his wife, Anna B., live at 1000 Forest Ave., Wilmette, Ill.

► *The Joint Committee* of the American Hospital Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS will meet in Washington on January 31.

► *Institutes* sponsored by the American Hospital Association in cooperation with the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS will be held this year in Chicago and Philadelphia. The one at Chicago will be held at the University of Chicago, June 16-20. The second Institute will be held at Temple University in Philadelphia, July 28 - August 2.

► *Colonel Leonard P. Zagelow* has been appointed chief of the Medical Service Corps of the U.S. Air Force. Colonel Zagelow is a pharmacist having received a Bachelor of Science and Pharmaceutical Chemistry Degree from Washington State College, and a Master of Science Degree in Pharmaceutical Chemistry and Pharmacology from the University of Minnesota.

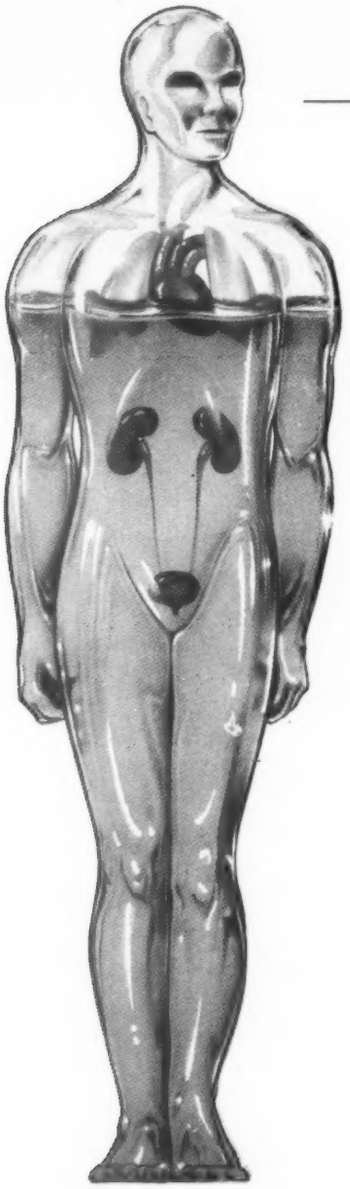
► *The Catholic Hospital Association* will hold its Annual Convention in Atlantic City, New Jersey, June 21-26.

NEW

'DIURIL'

(CHLOROTHIAZIDE)

a major breakthrough in the management of EDEMA patients and



ADVANCE PUBLICITY—'DIURIL' is being introduced after many months of intensive publicity at key medical meetings all over the country. Physicians are waiting for 'DIURIL'.

TREMENDOUS MARKET—The unique properties of 'DIURIL' make it beneficial in congestive failure, premenstrual edema, edema of pregnancy, nephrosis, nephritis, cirrhosis with ascites, drug-induced edema and hypertension. These conditions may be serious and occur frequently in medical practice.

LONG-TERM THERAPY—Most of the conditions in which 'DIURIL' is indicated require prolonged treatment necessitating repeat prescriptions.

SATURATION PROMOTION—'DIURIL' is being introduced with the most extensive detailing, direct mail, and journal advertising campaign ever put behind a Merck Sharp & Dohme product. Stock early and adequately.

SUPPLIED: 250 mg. and 500 mg. scored tablets of 'DIURIL' (Chlorothiazide) in bottles of 100 and 1,000.

HYPERTENSION patients

MERCK SHARP & DOHME
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Essential Facts about 'DIURIL' in Edema

'DIURIL' is the first of a new class of non-mercurial, orally effective compounds—one gram of 'DIURIL' orally being approximately equivalent to 1 cc. of mercurial I.M. 'DIURIL' is ideal for initiating diuresis and for prolonged maintenance of the edema-free state. It promotes balanced excretion of both sodium and chloride. Acidosis is most unlikely since the effect of 'DIURIL' on bicarbonate excretion is minimal. Increasing the dose of 'DIURIL' within recommended dosage range, increases diuretic response. 'DIURIL' is well tolerated even at maximum therapeutic dosage. It acts rapidly and its moderate duration of action permits uninterrupted rest at night. 'DIURIL' has no known contraindications.

DOSAGE RANGE: one 500 mg. or two 500 mg. tablets 'DIURIL' once or twice a day.

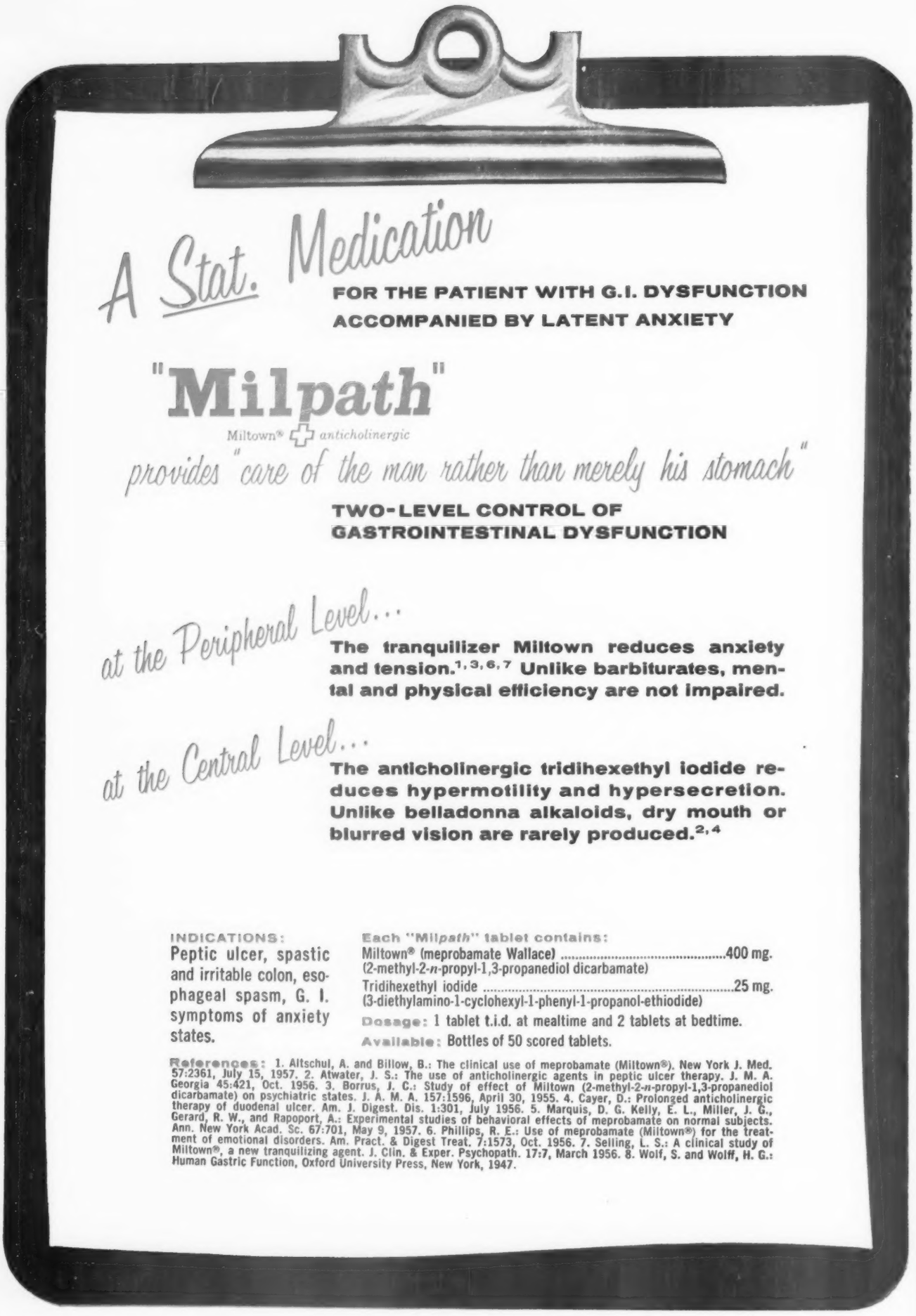
REFERENCES: Baer, J. E. *et al.:* Fed. Proc. **16**:278 (March) 1957; Beyer, K. H. *et al.:* Fed. Proc. **16**:282 (March) 1957; Ford, R. V. *et al.:* M. Rec. & Ann. **51**:376 (April) 1957; Ford, R. V. *et al.:* Arch. Int. Med. **100**:582 (Oct.) 1957; Ford, R. V. *et al.:* Antibiotic Med. & Clin. Therapy (in press); Moyer, J. H. *et al.:* Proc. Soc. Exper. Biol. & Med. (in press); Novello, F. C. and Sprague, J. M.: J. Am. Chem. Soc. **79**:2028 (April 20) 1957; Russo, H. F. *et al.:* Fed. Proc. **16**:333 (March) 1957.

'DIURIL' in Hypertension

'DIURIL' provides basic therapy to improve and simplify the management of hypertension. It potentiates the antihypertensive agents, frequently reducing their dosage requirements below the level of more serious side effects. 'DIURIL', added to the regimen, is often effective in controlling the blood pressure of even highly resistant or malignant cases of hypertension. 'DIURIL' maintains its effectiveness even during prolonged use. It smooths out blood pressure fluctuations due to ganglionic-blocking agents, thus improving the well-being of patients receiving these agents. 'DIURIL' is easily administered orally, with simple, effective dosage schedules.

DOSAGE RANGE: 500 mg. to 1500 mg. per day, given in divided doses (B.I.D. or T.I.D.).

REFERENCES: Hollander, W. and Wilkins, R. W.: Boston Med. Quart. **8**:69 (Sept.) 1957; Freis, E. D. *et al.:* J.A.M.A. (in press); Finnerty, F. A.: N. Y. State J. Med. **57**:2957 (Sept. 15) 1957; Freis, E. D. and Wilson, I. M.: Med. Ann. District of Columbia **26**:468 (Sept.) 1957; Freis, E. D. *et al:* Circulation (in press).



A Stat. Medication

FOR THE PATIENT WITH G.I. DYSFUNCTION ACCOMPANIED BY LATENT ANXIETY

"Milpath"

Miltown® + *anticholinergic*

provides "care of the man rather than merely his stomach"

TWO-LEVEL CONTROL OF GASTROINTESTINAL DYSFUNCTION

at the Peripheral Level...

The tranquilizer Miltown reduces anxiety and tension.[1,3,6,7] Unlike barbiturates, mental and physical efficiency are not impaired.

at the Central Level...

The anticholinergic tridihexethyl iodide reduces hypermotility and hypersecretion. Unlike belladonna alkaloids, dry mouth or blurred vision are rarely produced.[2,4]

INDICATIONS:
Peptic ulcer, spastic and irritable colon, esophageal spasm, G. I. symptoms of anxiety states.

Each "Milpath" tablet contains:
Miltown® (meprobamate Wallace) ..... 400 mg.
(2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate)
Tridihexethyl iodide ..... 25 mg.
(3-diethylamino-1-cyclohexyl-1-phenyl-1-propanol-ethiodide)

Dosage: 1 tablet t.i.d. at mealtime and 2 tablets at bedtime.

Available: Bottles of 50 scored tablets.

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**Elman, R.: Protein Needs in Surgical Patients, J. Am. Dietetic Assn. 32;524 (June) 1956.*

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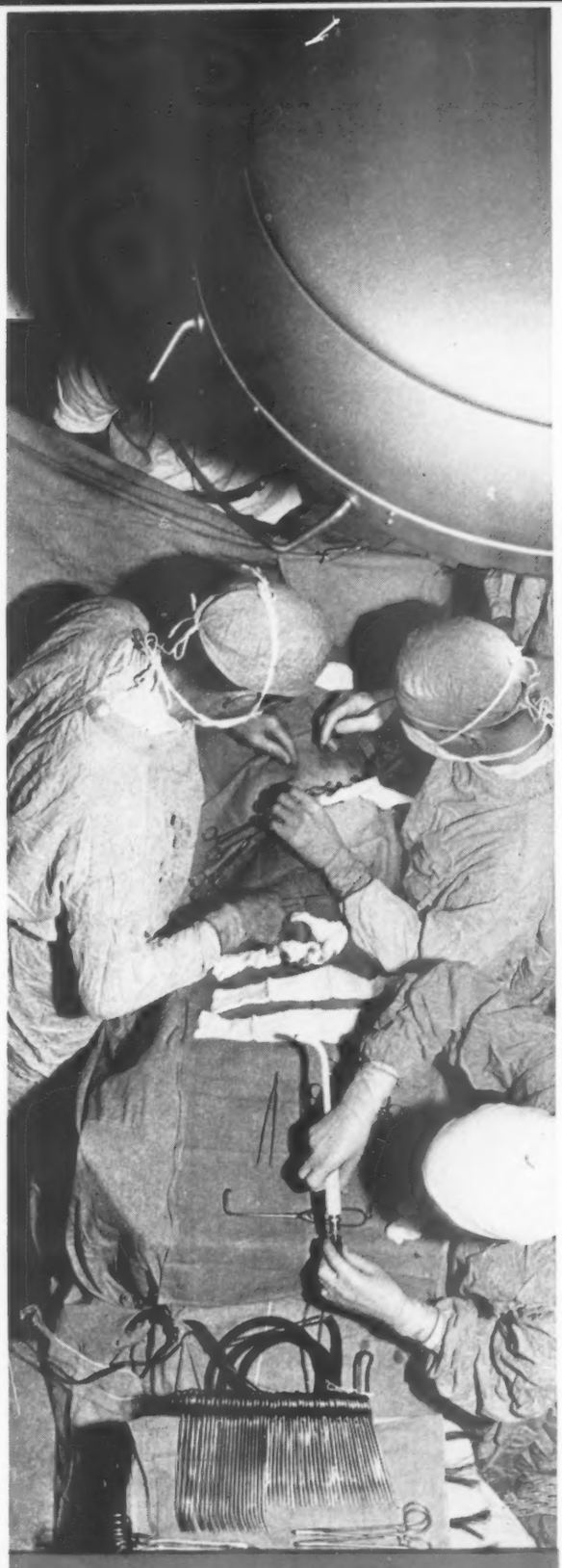
1. Dripps, R.C.: Hazards of the Immediate Postoperative Period, J.A.M.A. 7:795 (Oct. 19, 1957). [This reference reviews postoperative hazards, and does not refer to Adrenosem Salicylate].



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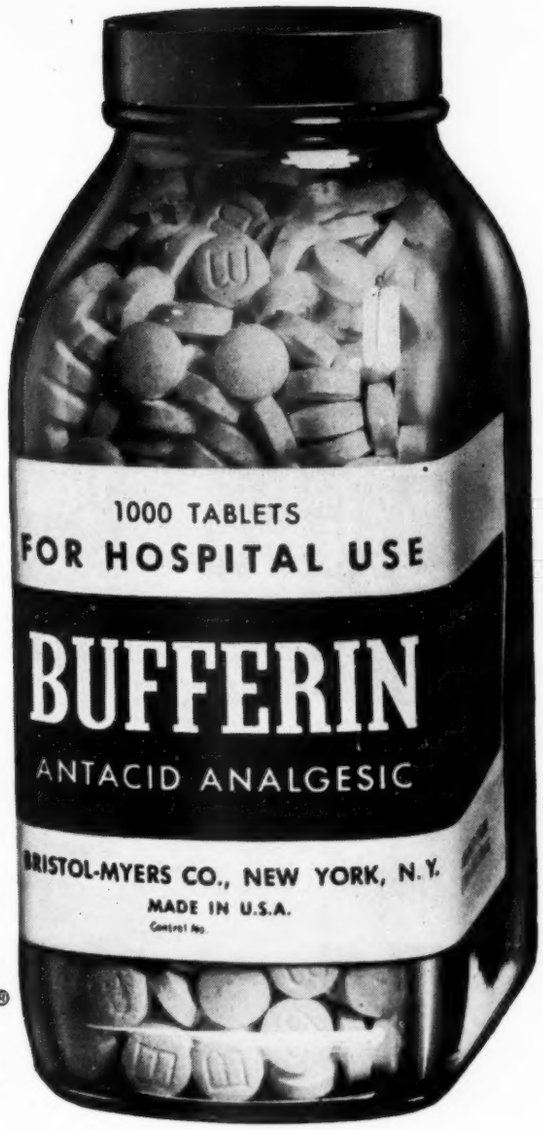

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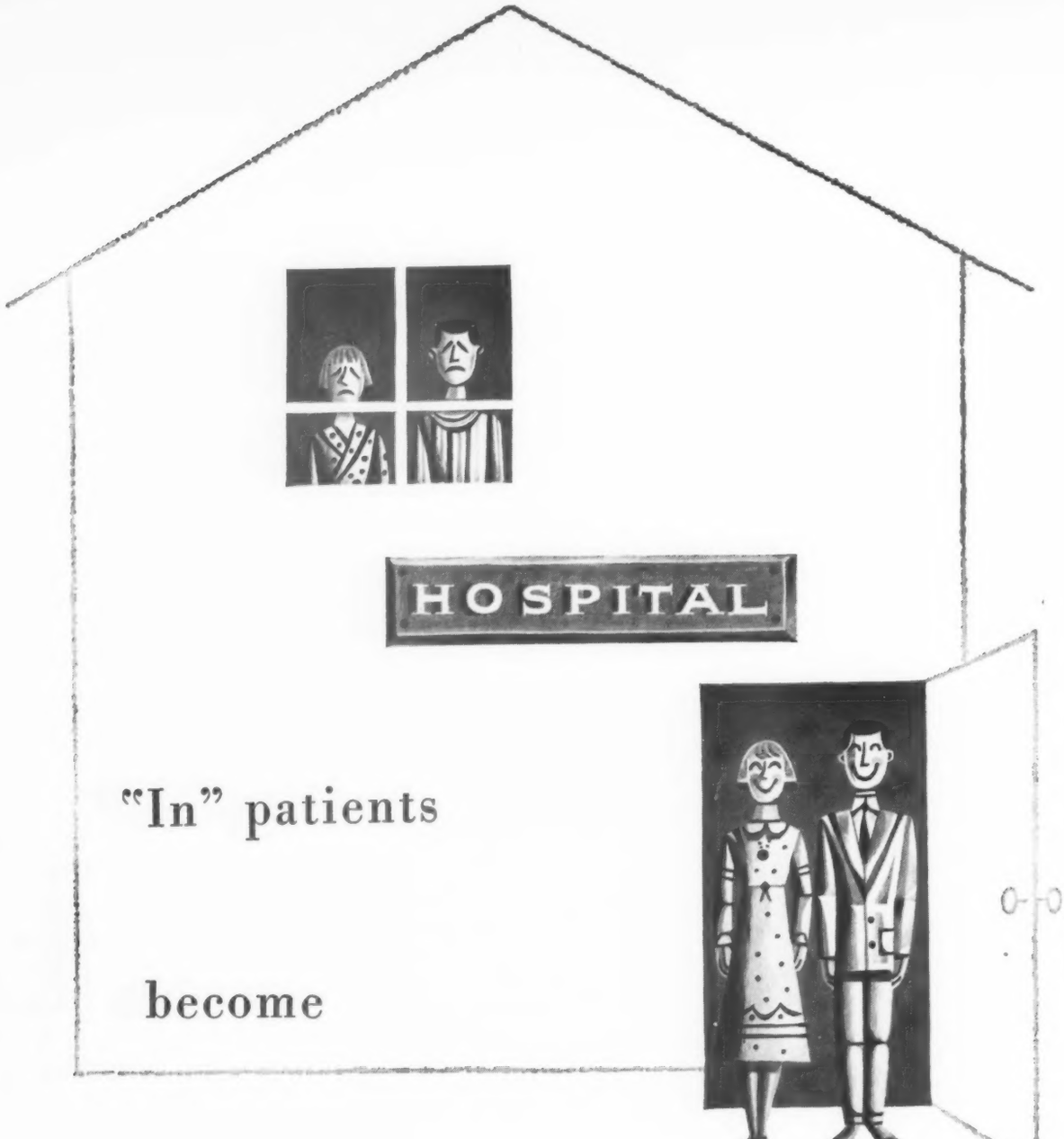

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Dear Sirs:

Sampling Parenteral Solutions

DEAR SIRS: Your editorial on Parenteral Solution preparation in the current issue of THE BULLETIN moves me to some comment. The sampling of hospital prepared parenteral solutions was not sufficiently large to permit reliable percentage expression, as admitted by the authors. Obviously though, a random sampling turned up too many off-standard samples.

In your editorial you attempt to point to a similar fallibility on the part of professional manufacturers and use the figure of 20 percent on the basis of 1 out of 5 samples being outside of specified limits. The figure could be a true one but is awfully shaky to predict with so few samples. According to statistical tables, with 5 samples a 90 percent or better confidence limit says that 1 out of 5 could represent between 2 percent and 67 percent.

The review of this situation is very good and should serve to have some people do some control work.

PAUL E. NORRIS

Drug Products Division
The Procter & Gamble Company
Cincinnati 17, Ohio

Correction

DEAR SIRS: In the September-October issue of THE BULLETIN, under the article, "A Study of Parenteral Solutions Made in Hospitals," I note that you identify Dr. Belcastro, one of the co-authors, as a graduate student at the time the work reported in the paper was done.

Actually, Dr. Belcastro should be listed as Assistant Professor of Pharmacy at Purdue University. It was he who really initiated the project and he acted as co-director of Miss Olynyk's work. I would like him to receive full credit for his valuable aid in directing the work and preparing the paper for presentation.

GLEN J. SPERANDIO, *Associate Professor of Pharmacy*

Purdue University
School of Pharmacy
Lafayette, Indiana

Aminopterin as an Abortifacient

DEAR SIRS: There have been some articles in lay publications about the use of the drug aminopterin as an abortifacient. These stories have not given all of the facts (insofar as we now know them) and we are concerned that those in the health professions may not be fully informed about the hazards of such use of this drug.

As you know, this drug was released for use in acute leukemia in children. The labeling to which we agreed in no way suggests that the drug may be used for therapeutic abortion, and in fact carries a warning that it should not be administered to pregnant women. Entirely aside from any legal or moral considerations, the facts we now have certainly indicate that the label warning should be observed. In the first place, the drug when given in the dosage and duration necessary to cause abortion is a threat to the life of the mother. In addition, when used to induce an abortion the drug is not quick acting or positive in its abortifacient effect, and the pregnancy may go to full term, or near it, and the child when born may well be a monster.

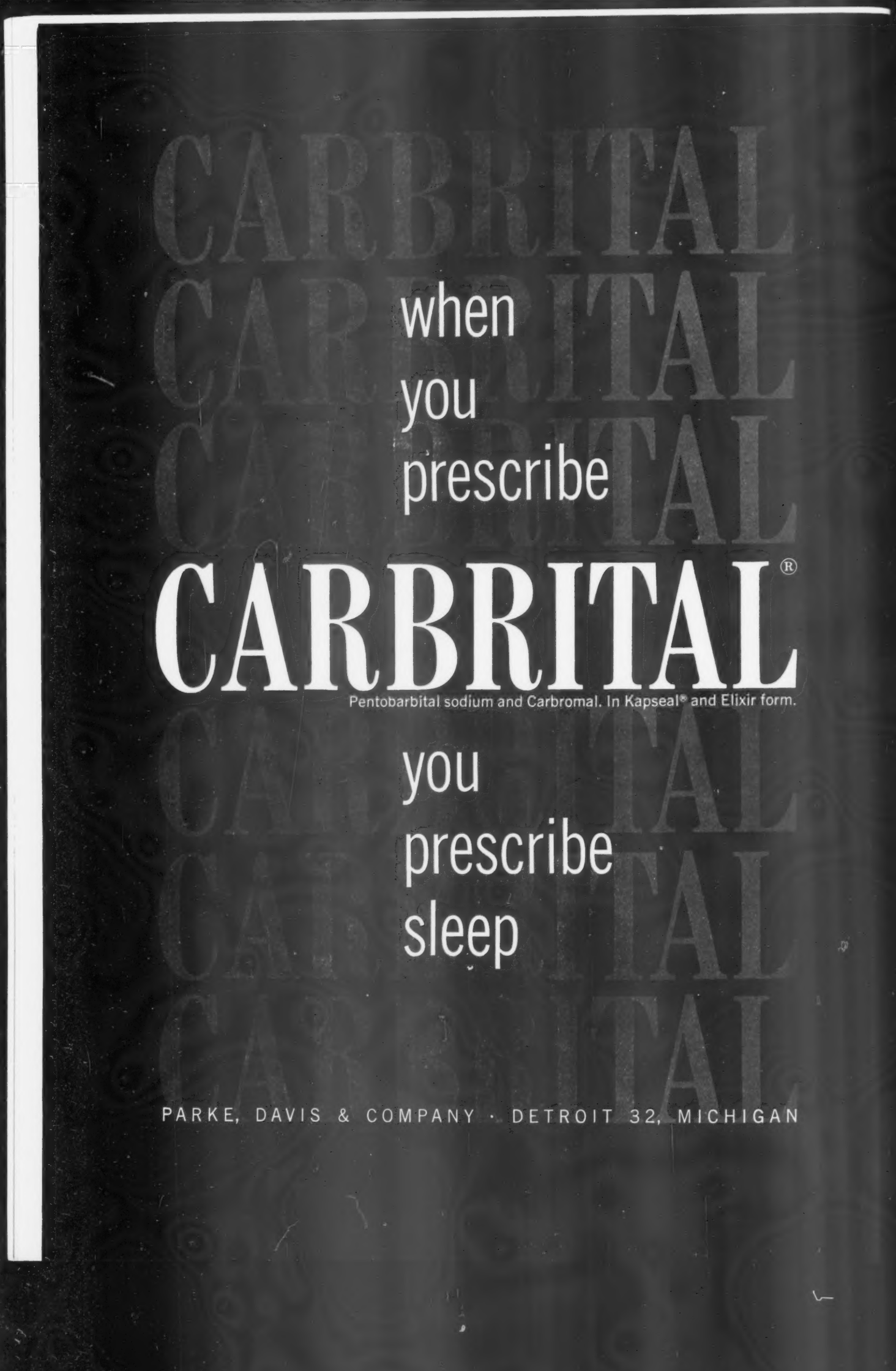
There have been to our knowledge a number of attempts to use this drug surreptitiously to cause an abortion. We have brought one prosecution case against a pharmacist who sold aminopterin without prescription for such use. The attempted abortion was not successful, but the woman was seriously injured, requiring hospitalization. The child was born at full term but died the following day. The cause of death was reported as "multiple congenital anomalies."

These facts if generally known might deter the most foolhardy from attempting to use this drug in secret, to cause an abortion, but we doubt that it would be wise to direct any publicity to the general public regarding this matter, since those to whom the publicity was directed might well remember only the fact that the drug may cause an abortion. We did think it would be well to alert pharmacists about this matter.

We solicit your assistance in disseminating the substance of this letter to pharmacists.

GEORGE P. LARRICK, *Commissioner of Food and Drugs*

Department of Health, Education and Welfare
Food and Drug Administration
Washington 25, D. C.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editorial

by DON E. FRANCKE

American Journal of Hospital Pharmacy

► APPEARANCE OF THE SOCIETY'S PUBLICATION on a monthly basis with a change in name and format is the result of thoughtful consideration and careful planning by members of the Executive Committee. The subject of a monthly publication has been discussed by the SOCIETY'S Executive Committee for a number of years. It was the opinion that the SOCIETY'S members could be better served by a monthly publication because under such a program it would be possible to publish more of the papers which are presented at the Institutes on Hospital Pharmacy, at the conventions of the ASHP, at conventions of the hospital associations, and at local and regional seminars. Also, a monthly publication permits more regular reporting of developments in new drugs, ideas for improved professional practice, and the numerous other items in which hospital pharmacists are interested.

The name of *The Bulletin* was changed to the AMERICAN JOURNAL OF HOSPITAL PHARMACY only after long and careful consideration. There was a certain reluctance to a change in the name because *The Bulletin* had become so well-known and accepted not only by American hospital pharmacists but by many in foreign lands. However, in spite of this, it was the concensus that the term "Journal" more accurately describes a publication of a national professional society and that the best time to make the change is now, when the format of the publication is being changed and as it goes on a monthly basis.

The present change represents another step in the development of the SOCIETY'S publication. In this connection it is interesting to note that there was no provision in the original Constitution and By-laws for a publication of the SOCIETY. Thus great credit is due Leo Mossman and the late Harvey A. K. Whitney (see page 2) for combining their efforts to put out a publication for the SOCIETY. The first volume, on green mimeograph paper and typed on an ordinary typewriter, appeared at irregular intervals during 1943-1944 and was known as the *Official Bulletin of the American Society of Hospital Pharmacists.* In 1945 the name of the publication was changed to *The Bulletin of the American Society of Hospital Pharmacists.* It was published in lithoprint form and issued on a bimonthly basis. During the next five years *The Bulletin* underwent minor changes in style and format but major changes were made in editorial content with several new sections devoted to items of special interest to hospital pharmacists being added and a larger number of major articles published. Beginning in 1950 *The Bulletin* was first issued in type-print form and advertising was accepted.

Throughout the years, the SOCIETY'S publication has contributed to the progress of hospital pharmacy in five major areas. It has fulfilled the everyday, practical needs of hospital pharmacists for information on administrative, technical, and professional subjects. It has provided a vital means of contact among hospital pharmacists and thus has removed their former feeling of isolation. It has greatly broadened the perspective of hospital pharmacists, giving them a truer realization of their role in the hospital and their importance as department heads. It has stimulated and otherwise encouraged hospital pharmacists to prepare scientific articles for publication, to undertake investigations of various types, and to engage in a broad range of professional activities which have raised the status of hospital pharmacy practice. And it has brought to hospital pharmacists a sense of unity and of progress by providing a publication which reflects their hopes and aspirations and by recording the many significant advances which hospital pharmacists have been able to make through cooperative efforts within the framework of the SOCIETY and the Division of Hospital Pharmacy.

The objectives of the AMERICAN JOURNAL OF HOSPITAL PHARMACY remain much the same as those of *The Bulletin.* It is the hope of the editorial staff that the issuance of the SOCIETY'S publication on a monthly basis will make it possible to provide greater service to all hospital pharmacists in the interest of better patient care and for the betterment of our profession.

MICROCOCCUS PYOGENES

La Bete Noire of the Hospital in Midcentury

by Robert A. McAlexander *and*
J. Thomas Payne

► A DECADE AGO, THE GOLDEN AGE OF SURGERY had arrived. It seemed possible to completely eliminate the wound infection as a complication of the brilliantly executed surgical procedure. Post-operative pneumonia, it was hoped, would no longer occur. The surgeon and his colleagues could devote their efforts to conceiving and carrying out an increasing number of corrective procedures with the patient and his physiology and anatomy as the main problems. Antibiotics gave great promise.

For four or five years this euphoric state pervaded the clinics of the world. Antibiotics were first given to eliminate infections present, then to abort impending infections, and finally to prevent infections which might possibly occur in the future. Abuse of old antibiotics was somewhat offset by the development of newer ones. A few[1] predicted that this happy state of affairs could not last.

Now, within the professional lifetime of a third year medical student, the microbiologic picture of surgery has very nearly returned to its pre-antibiotic state of the early "forties." The elective operative wound developing an infection is commonplace on hospital wards. Fulminating wound infections progressing rapidly to bacteremia and death occur in epidemics through the world.[2,3] Post-operative pneumonia, often fatal in result, is found wherever one wishes to look objectively. Antibiotic creation is barely keeping abreast of antibiotic resistance. The situation is becoming increasingly serious.

It is the purpose of this paper to relate certain experiences with this problem of infection in the surgical patient and to suggest techniques which may be helpful in handling such problems.

Robert McAlexander B.S. is a Senior in the School of Medicine, University of Washington, and J. Thomas Payne, M.D. is associated with the Department of Surgery, School of Medicine, University of Washington and The Polyclinic, Seattle.

Presented at the Institute on Hospital Pharmacy, Seattle, Washington, June 26, 1957.

The Organism

Whether by relative importance or by actual numerical frequency, the only organism of significance in the international surgical picture is the *Micrococcus pyogenes*. The streptococcus plays little or no part in the usual surgical infection. It has served only occasionally as a cause of bacterial endocarditis in the patient who has undergone cardiac surgery. Seldom is it seen as a wound contaminant.

The coagulase positive *Micrococcus pyogenes,* however, is the organism which is the most frequently recovered. The organism can be typed by phage type or more readily by its resistance pattern to antibiotics, as determined *in vitro*.[4] (Figure 1.) Whether this organism develops as a result of overgrowth, genetic change, superinfection, or contamination of wound or tracheobronchial tree is of no moment. It is the one that always appears and it is the one that is pathogenic.

The Clinical Entity

Staphylococcal infections appear in four forms with minor variations in individual hospitals.

1. The isolated wound infection seen in the surgical patient, which usually appears after the patient leaves the hospital.

2. The epidemic of wound infections deep and unrecognized which are often fulminating and lethal, and are very spectacular to all concerned.

3. The day to day infections seen in hospitals and accepted as unavoidable complications. These vary from "diaper rash" in the nurseries, to "terminal bronchopneumonia" seen in the elderly derelict and in the morgue.

4. The sporadic epidemics of "colds" and "sore fingers" seen in personnel working in hospitals and clinics.

1. The isolated wound infection usually appears within 4 to 5 days after the surgical procedure. In private institutions where such procedures as herni-

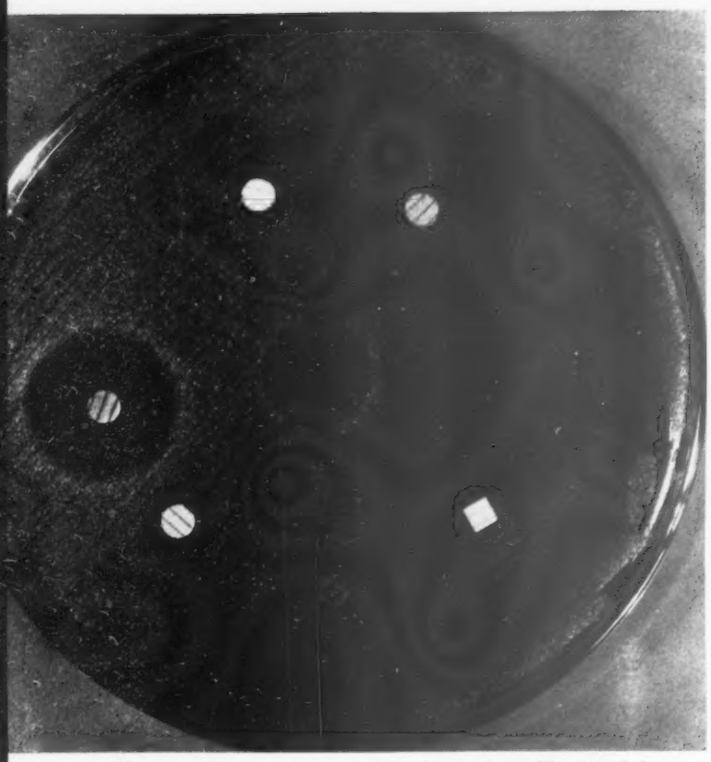

Figure 1. Micrococcus pyogenes is most readily typed by its resistance pattern. This plate is a typical grouping of antibiotics grown on a pure culture of the local strain. The organism is resistant to penicillin, streptomycin, tetracycline and sensitive to chloramphenicol, erythromycin, and novobiocin

orrhaphy, etc., merit only 2 to 3 days hospitalization, the patient is home when this appears. He is followed in his physician's office often for weeks—he, discontent with the surgeon's skill and the surgeon, discontent with his bad luck. The surgeon does not tell his colleagues about this ill fortune and his colleagues do not tell him of their similar cases. The empty ritual of hospital records and audits shows nothing and the hospital administrators are unaware of the epidemic. Such a patient is exemplified by this report.

A 22-year old man underwent excision of an enchondroma of the left fourth finger on May 28, 1957. The procedure was uneventful. The patient went home on May 29, 1957. On June 6, 1957 he noticed the wound was swollen and bluish in color. He attributed this to having struck the hand. On June 7, 1957 he was seen in his surgeon's office. This "hematoma" was drained, and cultures showed *Micrococcus pyogenes* resistant to penicillin, streptomycin, erythromycin and sensitive to chloramphenicol. He was treated for six weeks for this infection. The hospital record was corrected to show post-operative wound infection but the record librarian "corrected" this. Simultaneously, three other surgeons had similar experiences. The hospital administrator was polite but denied that this was a hospital problem.

2. The second type of infection is the virulent epidemic of deep wound infections which progresses to staphylococcemia and carries a high mortality.

At a large urban hospital, during the period from April 10 to 25, 1955 nine major procedures were done in the operating suite, by the same team of physicians and nurses. The patients did well for 24 to 48 hours, then one by one developed fever without any obvious wound infections. After several days of fever, the wounds of some were opened disclosing deep necrotizing infections and in some instances, empyema. From these wounds the hospital type of *Micrococcus pyogenes,* resistant to penicillin and streptomycin, was cultured. All had similar resistance patterns. On April 25, nine such patients were found on the surgical service. The operating room was closed. Four of these patients died in the next two weeks, and one died six weeks later. Of those who died all had been seriously ill prior to their operations and were not in optimum physical condition at the time of surgery. They all died with staphylococcemia, resistant to all antibiotics. At the time the operating rooms were closed and a search was made for the organism in the rooms and on personnel. It narrowed down to one nurse who had been having recurrent paronychia treated intermittently by her private physician. The paronychia had subsided but she had been plagued with recurrent auxiliary and inguinal furunculosis. Cultures from these lesions showed organisms with resistance patterns similar to those isolated from earlier and subsequent infected wounds. (Figure 2)

3. The day to day minor hospital infections seldom excite much interest until someone becomes aware of the total picture.

In July, 1954 a male infant was born after a normal pregnancy, to the wife of a physician. The family already had three daughters, so the event, while a routine one to the hospital, caused much excitement in the family. Three days after delivery, and with the remnants of the umbilical cord still attached, the infant went home with the mother. Upon arrival at home he was found to have a "diaper rash" which was characterized by several minute pustules over the inguinal region. (These were mentioned in the nurses notes on discharge.) The "rash" spread despite the fact that the diapers were washed in different soaps, and finally no diapers were used. Seven days post-partum the mother developed a painful, spreading mastitis on the left which went on to suppuration. Organisms cultured from this abscess and the pustules on the infant proved to be identical micrococci with similar resistant patterns. No antibiotics were effective. The mother finally placed both herself and the infant in the bright sun for 6 to 8 hours a day—he without "bottoms" and she without "tops' and both healed rapidly.

This episode became the subject of conversation between the physician and his friends. Four other such minor mother-infant epidemics from this hospital were discovered. Independently, other physicians discovered this spread of antibiotic-resistant organisms. Finally, a survey of this problem was made in this hospital (and others) by Ravenholt and LaVeck, who reported as high an incidence as "37 percent of infants and 13 percent of mothers had a suppurative illness following discharge from the hospital!"[5]

Another type of problem is exemplified by the 93-year old alcoholic recluse who fell, fracturing the left hip, and was brought to a local hospital 24 hours after the injury in a disoriented state. The fracture was reduced and nailed; however, the patient continued in a stuporous state. Despite an indwelling urinary catheter his blood urea nitrogen remained at about 60 mg. percent. He developed rales in both lung bases, and refused to eat. A feeding gastric tube and intravenous needles could not be kept in place. He died on the 14th post-operative day. He was signed out as uremia secondary to nephrosclerosis, hypertensive, and arteriosclerotic cardiovascular disease and bilateral terminal bronchopneumonia. This might well have been the end of

another senile derelict passing on in an acceptably routine manner, but for the fact that six other elderly persons in poor nutrition had died that same month. All seven patients had "terminal bronchopneumonia" and from all of the lungs, the hospital staphylococcus was cultured!

Death comes to the aged once more in the form of the "old folks friend" but now it comes from organisms given to them by their therapeutic environment. Wysham and Kirby[6] have documented this manifestation of the hospital staphylococcus. They have demonstrated that the aged, the diabetic, the patient in poor nutritional state, all are usually susceptible to the hospital infection. In fact, they constitute a far greater problem than do surgical wounds and skin eruptions, for the infection in the "poor risk" patient is subtle. It is apt to be taken for granted—accepted and overlooked. Yet when all else is under control, it is a tragedy to lose a patient by having a hospital incurred infection tip the balance.

4. The sporadic epidemics of colds are known to offices, factories, hospitals, and all places where humans work in groups. The complicating factor in the hospital is that from 15 to 65 percent of personnel are carriers of the specific type of antibiotic-resistant staphylococcus epidemic in that particular hospital.[7] Thus these people, when they get an infection, become carriers of virulent forms of micrococci.

Another form of infection is the paronychia. A pretty 23-year old nurse on a surgical ward in a federal hospital trimmed her cuticle one night while on night duty. Within 36 hours she had an angry, draining paronychia of one index finger. Culture of the pus showed the hospital staphylococcus. She was transferred to a ward of convalescent patients where she continued to work at night, treating the finger with soaks and chloramphenicol. The infection cleared very slowly. Within a week a patient who was being fitted for two artificial limbs on that ward developed an abscess of his back; another who was awaiting transfer to an old soldiers' home developed an abscess of the back of the neck, (Figure 3) and a third convalescent hemiplegic developed furuncles over the buttocks. The organisms from these abscesses were similar in resistant patterns to those isolated from the finger of the nurse. The epidemic died down coincident with the healing of all of these infections.

The Mechanism of Spread

The appearance of antibiotic-resistant micrococci over the world has been simultaneous with the universal use of antibiotics. It has been shown that these organisms are predominantly endemic in hospitals though some clinics and private offices report an increasing incidence. It has furthermore been well demonstrated by Knight and his associates that patients and personnel alike, upon entering the hospital environment, rapidly pick up the hospital micrococci.[8] The actual means by which these organisms are carried and transferred is undetermined as yet.

A survey was done during the summer of 1956 at the Seattle Veterans Administration Hospital in an attempt to find the intermediate steps of transfer of the organisms from carrier to patient. The most reliable method of typing of the staphylococci seemed to be by the antibiotic-resistance patterns. Using this method, 194 strains were identified among the patients and staff members, and four out of every five patients harbored pathogens. They were most frequently found in the nasal vestibule, then the hands,

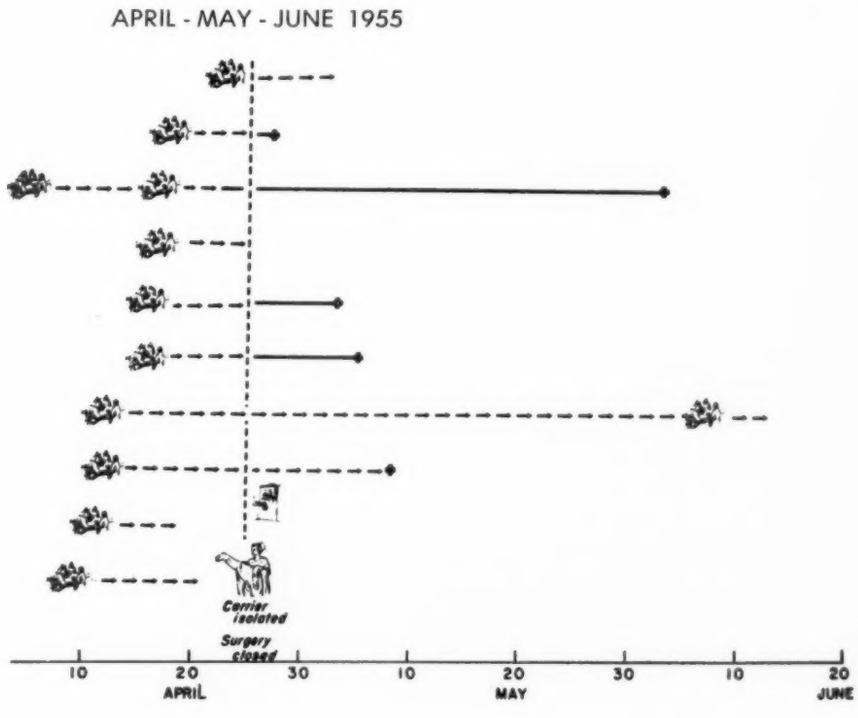

Figure 2. A chronology of an epidemic of deep wound infections occurring in a hospital. Five deaths out of ten patients concerned is a high price to pay for permitting a nurse to work because she wasn't "sick" though she was inconvenienced by inguinal furuncles. A step in preventing such tragedies is to give leave with pay to personnel with known staphylococcal skin infections.

wrists, and abdomens (only the patients' abdomens were cultured). The mouth yielded only occasional pathogens. Certain individuals were persistent carriers of pathogens and others carried them not at all or intermittently. Bedding was frequently heavily contaminated with pathogens, whether it was freshly laundered or not. The bedding appeared to be the site of initial acquisition by the patient and subsequent transfer to other patients.

From this work and the work of Knight[8,9] and Wysham[6] it is reasonable to assume that pathogenic staphylococci are transmitted to patients shortly after their admission to the hospital by direct contact with bedding and, to a degree, with the staff carriers. The hospital micrococci have a vitality which causes them to exist with non-pathogens even though they are probably outnumbered six to one (by our own figures). That they can be air-borne from the wards to the operating rooms has been nicely demonstrated by Shooter and his associates who reduced the incidence of wound infection from nine to one percent by simply reversing the flow of air so that it went from operating suite to ward.[10] The virulence of a pathogen and its chief danger comes when it produces an infection which comes over the clinical threshold (*e.g.* the paronychia, or "cold"). The organism from this lesion has a dangerous potential whereas the one from the casual asymptomatic carrier is benign, in our experience.

Starkey[11] has demonstrated that modern hospital cleaning methods are as yet inadequate to remove staphylococci from hospital dust and fomites, and until hospital equipment and design can overtake the ubiquitous staphylococcus, the chain of dissemination must be broken at its source. Duguid and Wallace[12] have shown how the nasal staphylococcal carrier showers the organisms on his environment from his clothing as he moves, and there is much evidence suggesting the main reservoir of staphylococcal carriage is in the nose. We feel that prevention of spread from this site would eliminate the main source of ward contamination resulting in the *occasional* sporadic case of hospital infection. Hospital personnel should be instructed to blow their noses on disposable tissues by a wash basin, and to immediately wash their hands, just as if they had been changing a contaminated dressing.

Control Measures

Several measures may help to control the spread and clinical effects of staphylococci in the hospital.

1. Hospital personnel must be informed of the problem of staphylococcal infection and the role of the nasal vestibule, the hands, and the blankets and bedding as reservoirs for widespread dissemination.

Requiring particular emphasis is the importance of reporting, culturing, and adequately treating infections of nose and throat and skin occurring in hospital personnel. The hospital administration should, without hesitation, place a worker with a symptomatic infection on leave with pay or in a non-clinical position until the infection is asymptomatic (which is for

Figure 3. This abscess occurring on the back of the neck in a convalescent patient contained the same organisms as were cultured from a paronychia of a nurse who had been transferred to the ward to "get over" her infection

practical purposes coincident with cessation of the high pathogenic state).

2. Patients with infections must be isolated to prevent air-borne infection of other patients and ward fomites. This isolation must be observed by all, not just the lower echelons of personnel as is commonly the case.

3. In the operating rooms, a revival of the basic principles of asepsis and good surgical technique is required. Study of traffic patterns and ventilation should be done to ensure reasonably safe personnel and air flow.

4. The use of prophylactic antibiosis should be kept to a minimum. The Tenants of Altemeier[13] are probably the most reasonable and if possible, every staff member should be "sold" on these. In civilian surgical practice prophylactic antibacterial agents should be limited to use:

> "a. In contaminated wounds of violence.
> b. In elective surgical procedures performed through or in contaminated areas such as the gastrointestinal, respiratory or genitourinary tracts.
> c. In patients with associated derangements of the urinary tract who undergo surgical operations.
> d. In patients with indwelling catheters.
> e. In persons with pre-existing valvular heart disease who sustain injuries or undergo operations of the oral or pharyngeal cavities.
> f. In patients undergoing emergency surgery in the presence of associated but not unrelated infections such as acute tonsillitis.
> g. For preparation of the gastrointestinal tract.
> h. For elderly people with chronic pulmonary disease who undergo surgical treatment."

5. Finally, the success of any program instituted to reduce hospital infections depends on effective monitoring, with cooperation of all concerned, by simple epidemiologic studies of *each* infection or group of infections. Communication is the key to this, and the argument as to whether the infection appeared in or out of the hospital has no place in this study.

Summary and Conclusion

One of the most serious problems of medicine today is the hospital incurred infection due to antibiotic-resistant *Micrococcus pyogenes*. This is a problem for all hospitals and its magnitude is realized only when it is searched for and defined. Four manifestations can be recognized: (1) The isolated wound infection appearing in the surgical patient, often after he leaves the hospital; (2) The epidemics of deep, severe wound infections which go on to staphylococcemia and death in over half of the patients; (3) The day to day infections such as pyodermia in the nursery, mastitis in the mother, "terminal bronchopneumonia" in the aged and critically ill; and finally (4) Sporadic epidemics of minor infections in hospital personnel. Any one of these manifestations can lead to death of a patient. The antibiotic-resistant micrococcus is endemic in hospitals. Only about 15 percent of the strains are virulent and the *most* virulent strains are those coming from a person with an infection above the symptomatic horizon. Patients rapidly pick up the hospital strains of organisms, even though their own strains outnumber the hospital ones by six to one. Bedclothes, the nasal vestibule, and the hands and wrists of hospital personnel are the most common reservoirs. Transmission can be by direct contact or by air draughts. Control measures are best carried out by a staff educated to the problem. The isolation and treatment of the carrier of the virulent strain is the most important single measure. Economically this may be temporarily expensive but clinically it is sound. Finally, the use of antibiotics should be reserved for specific conditions soundly reasoned and, if possible, documented by culture and sensitivity studies.

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certain aspects of

RADIOLOGICAL HEALTH

by WILLIAM H. BRINER

► IN THE RELATIVELY SHORT PERIOD OF eleven years since the Manhattan Engineering District first released certain by-product material, known as radioisotopes, from nuclear reactors for civilian applications, there has been a rather profound and, at times, sensational increase in the number of articles appearing in the literature concerning the use of these materials. Recently, as a result of Congressional hearings, the scrutiny of the American press and public has been directed and rightly so, to the concern exhibited by a number of the nation's leading scientists with regard to the possible deleterious effects of large scale exposure to these radioactive substances.

Unfortunately, not in all cases has the deluge of writing which has appeared been scientifically accurate. Indeed, one might almost conclude that there seems to be an inverse relationship between the numbers of the populace exposed to such journalistic efforts and the credibility of their contents.

When dealing with so important an aspect in the daily lives of all of us, the impact of such confusing opinions and reports upon an uninformed or, at best, misinformed public can only be disasterous. Since one of the distinguishing characteristics of a professionally trained individual certainly must be the ability to think objectively, weigh the evidence available and then submit an opinion based upon these truths, it is in this area of objectivity that the professional people of this country can best serve the interests of the nation as a whole in the matter of radiological health.

For the most part, the literature of hospital pharmacy, perhaps quite logically, has been concerned with certain medical uses of radioisotopes, both diagnostic and therapeutic, which have gained wide acceptance in hospitals throughout the country. On the other hand, with a very few exceptions, there has been a notable lack of writing within the profession concerning some of the more basic considerations in this field.

This presentation is by no means intended to be a comprehensive discussion of nuclear energy and its applications, either medical or otherwise. Rather, its purpose is to provide a source of information for the practicing hospital pharmacist which will enable him to discuss a bit more intelligently with other members of the health professions and the laity alike this exciting and important area of endeavor, and to better understand the magnitude of the problem which confronts the agencies who would control the use of radioactive substances in this country.

Fundamental to an understanding of any technical field is a knowledge of the terminology and vocabulary encountered in the literature peculiar to that particular science. Radioactivity itself refers to the several processes by which atomic nuclei spontaneously decay or disintegrate by one or more discrete energy levels or transitions, until, ultimately, a stable state is reached. This decay of which we speak, then, gives

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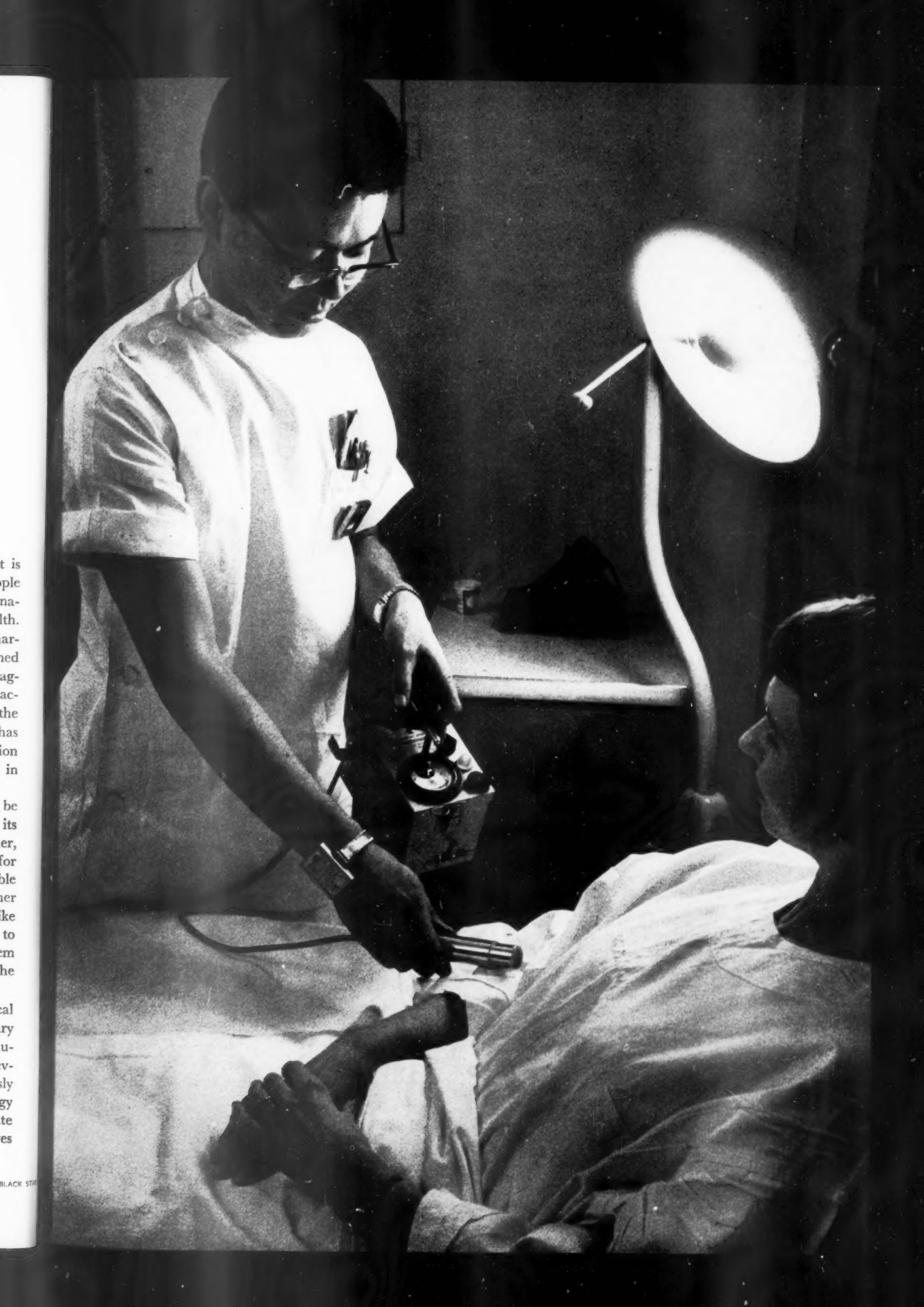

rise to the radioactive emanations capable of producing rather remarkable effects in any medium with which they react.

Early Work

Notable in the early investigations in the field of radioactivity was that of the French physicist Henri Becquerel who, in 1896, demonstrated that a uranium ore caused darkening on a photographic plate, which was shielded with opaque paper, in much the same manner as x-rays. This was the first reported evidence of what has come to be known as "natural radioactivity." Subsequent investigations proved that numerous elements above atomic number 82 shared this ability with uranium.

The New Zealand physicist Ernest Rutherford, in 1903, further defined the properties of radioactivity by demonstrating that there are three kinds of radioactive "rays": alpha, beta, and gamma.

More extensive research has since qualified Rutherford's work by defining the basic difference between the two general types of radiation as we know them today, namely particulate and electromagnetic. It must be mentioned at the outset, disconcerting though it may seem, that under certain circumstances no truly definitive line may be drawn between the particulate and electromagnetic properties of radionuclides. That is, both particle properties and wave properties may be exhibited. This seeming inconsistency has been termed "wave-particle duality" and is mentioned only to preclude an unwanted and incorrect impression that this difference is always a clear-cut one.

Particulate radioactive emanations include alpha particles, beta particles, and positrons, while the connotation electromagnetic is given to gamma rays.

Properties of Particles

It may be well, at this point, to discuss briefly some of the properties of these several types of emissions. Alpha particles are found in the decay schemes of only relatively heavy radioisotopes. They are the least penetrating of the three types of radiation. In fact, they may be stopped by a piece of paper or a few centimeters of air and are of little concern as an external radiation hazard. However, since alpha particles have a high specific ionization value they constitute the greatest hazard when they find their way into the human body. Since alpha particles are composed of two neutrons and two protons, they have two unit positive charges and a mass of four atomic mass units. Thus, they are identical in structure with the helium nucleus and may be symbolized α, or $_2He^4$.

Beta particles, on the other hand, may be visualized as high speed electrons which originate in the nucleus. They have the same mass as an electron and bear a unit negative charge. Their penetrability is several hundred times that of alpha particles, so it usually requires the order of several millimeters of aluminum to absorb them. Although beta particles possess a somewhat lesser ability to ionize the medium through which they travel than do alpha particles, they may be quite hazardous within the body and, depending upon their energy, may constitute an external hazard as well. Beta particles are often symbolized β,β^-, or $_1\beta^0$. Positrons are similar to beta particles with the exception that they bear a unit positive charge. They are symbolized β^+. $_1\beta^0$, or $_1e^0$.

Finally, gamma rays are the most penetrating of the three radioactive emissions. A type of electromagnetic radiation, they move with the speed of light and are quite similar to x-rays, with which they differ chiefly in origin. It is theoretically impossible to completely stop or absorb gamma radiation, although it may be reduced in intensity to practical limits with such materials as lead. Gamma rays are the most hazardous with respect to external radiation and are symbolized by the Greek letter γ.

It is well to remember that, although emphasis has been placed on the inherent dangers of alpha and beta particles within the body, all radioactive emanations may be dangerous internally under given conditions. They differ only in the degree of that danger.

Transmutation

There are certain phenomena observed when radioactive nuclides decay or disintegrate. Of particular interest to pharmacists, since there are a number of alchemists in the heritage of our profession, is the fact that when a nucleus decays by alpha, beta, or positron emission, a transmutation occurs, and a new element is formed. For example, when lead-214 decays, the following reaction occurs:

$_{82}Pb^{214} \longrightarrow {}_{83}Bi^{214} + {}_{-1}e^0$ and an isotope of bismuth results. In writing nuclear reactions, the subscript refers to the atomic number, often called the "Z" number, while the superscript refers to the mass number or isotope number, which is also known as the "A" number. When transmutation takes place, the nucleus which is formed, and known as the "daughter," is usually radioactive and may attain a stable or ground state by the emission of a gamma photon.

Energies of Radiation

Each radioisotope has its own characteristic decay scheme which differs from the disintegration patterns of other radioisotopes in the types and energies of the emissions, and also in the rate at which these events occur. Energies of radiation are commonly stated in millions of electron volts (mev.). The energy of particulate radiations is manifest as kinetic energy of motion in contradistinction to electromag-

netic energy, which varies according to the wave length and frequency of the ray, since velocity is constant in all gamma rays.

The rate of decay for any given isotope is a constant value. This is to say that a certain number of radioactive atoms present decay per unit time and is known as the decay constant (λ) for the particular isotope. A term frequently used to describe the rate of decay of an isotope in a somewhat different manner is "half-life." Radioactive decay is not a linear function; rather, it is exponential and completely random in nature. Hence, one cannot say with any degree of certainty when any one radioactive nucleus will disintegrate. However, when a sufficiently large number of atoms of a radionuclide are present, the time interval required for half of these nuclei to decay may be stated with a good deal of accuracy. It is to this time interval which the name half-life has been ascribed.

Biological and Effective Half-Lifes

In addition to radiochemical half-life which has just been considered, there are two other half-life values of interest to the health professions. These are biological half-life, which is a statement of the amount of time required for the body to eliminate one-half of an administered dose of a substance by regular processes of elimination, and effective half-life, which is the amount of time required for the amount of a radioactive element fixed in the tissues to be reduced 50 percent due to the combined action of radioactive decay and biological elimination. It is interesting to note that there is seldom any significant difference in biological half-life between a stable and a radioactive isotope of a given element.

These decay constants, half-life values, and energies which we have been considering are so characteristic of each individual radioisotope that identification of an unknown isotope may be based upon these factors. There is no known manner by which the decay scheme of a radioactive substance may be altered.

The need for some sort of device to detect this source of energy known as radioactivity becomes apparent when one realizes that none of man's senses is capable of determining the presence of a radiation field. Inherent in this need for a means of detection is the necessity to have a system of units or dimensions in order that the intensity of the radiation might be stated in meaningful terms. Fundamentally, there are only two systems of units in the radiological health vocabulary. One of these is concerned with the quantity of radioactivity contained in a given sample of material, and the other attempts to relate quantity of activity with its effect on a biological system in terms of a dose or dose rate.

Units of Measurement

Quantity of radioactivity is commonly stated in curies, or sub-multiples of curies. These units are based on the number of atoms of a radioactive substance which are disintegrating per unit time and may be used for radionuclides which decay by alpha, beta, or gamma emission. The basic unit of dose is the roentgen, although it is specifically applicable only to gamma and x-radiation. The definition of a roentgen is rather involved and important only to those who work with nuclear energy. Suffice it to say that it is an expression of the degree of ionization of aid attributable to the effect of gamma or x-radiation, and that a transposition to an effect on tissue has been made. Since the roentgen is correctly applied only to electromagnetic radiation, it became necessary to derive a unit to express dosage from particulate radiation. Probably the most popular unit for this purpose is the *roentgen equivalent physical* (rep.). More recently, another unit has come into use which will eventually, because of its greater accuracy for stating biological doses, replace the rep. This unit is the *roentgen equivalent man* (rem.). Both the rep. and the rem. are units which are used to assess the degree of biological damage which results from the absorption of a given amount of radiation.

Radiation Detection Instruments

Radiation detection instruments may be sub-divided either according to the use to which they are put or with respect to the type of medium utilized in the detector. When classified according to use, they generally fall into one of three categories: survey instruments, personnel monitoring instruments, or laboratory instruments.

Survey instruments are usually portable, relatively simple in design, and may give a meter reading either in roentgen units per unit time, counts per unit time, or both. They are used to determine grossly the presence of a radiation field or radioactive contamination.

The two most frequently used personnel monitoring devices are film badges and pocket ionization chambers, often referred to as pocket dosimeters. Film badges are packets containing photographic films which exhibit a varying, but known, sensitivity to radiation of diverse energies. Upon developing, the degree of darkening of the films, as determined by an instrument known as a densitometer, gives a fairly accurate indication of the amount of radiation striking the badge, when compared with similar films exposed to known amounts of radiation. Pocket ionization chambers are small devices resembling fountain pens in appearance. As their name would indicate, the amount of ionization of an enclosed sensitive

volume of a gas is measured by a self-contained electrometer. Both the film badge and the pocket ionization chamber indicate a cumulative dose rather than a dose rate.

Finally, laboratory instruments are the most sensitive of the three types. This type of instrumentation is employed when an assay or calibration of a source of radioactivity is desired. The conditions under which these instruments are used lend themselves well to reproducibility of results, a factor which is seldom, if ever, attainable with other types of instruments or devices.

Scintillation Detector

When classifying radiation detection instruments with respect to the media they employ in this detection process, one might place them in one of five categories. In each instance, detection is possible only because of the ability of radioactive emanations to produce ionization of the medium with which they react. These five classes are gases, photographic emulsions, scintillators, chemical decomposition, and radiophotoluminescent substances. Two of these, the photographic emulsion and gas media, have been mentioned only briefly in the discussion of types of detection instruments, and certainly, space will not permit a detailed exposition of the three remaining media. However, a few words are in order concerning the scintillation medium, since it is so frequently encountered and versatile in its applications. Radiations are able to produce in certain chemical entities very minute flashes of light, or scintillations. In the circuitry of a scintillation counter, a photomultiplier tube picks up these scintillations, and, in successive stages, increases them in intensity until a measurable current pulse results. This current pulse, then, is indicative of the amount of radiation to which the instrument is exposed. Perhaps the chief advantage of a scintillation-type detector is that it may be adapted to any type of radiation merely by changing the phosphor, or chemical which emits these minute flashes of light. This ease of adaption is the exception rather than the rule in radiation measuring instruments.

Now that we have established the fact that radioactivity exists, defined it, and outlined means of detecting it, there remain the problems of how to protect one's self from its harmful effects and of fixing the limits of exposure of the human race to radioactivity at a reasonable level.

Radiation Protection

There are basically three principles used in radiation protection: time, distance, and shielding. In other words, decrease to the smallest possible increment the time during which exposure to a source of radioactivity takes place, increase as much as possible the distance from the source, and utilize proper absorbers or shields to diminish to a reasonable level the amount of radiation reaching the body. Usually, when working with a source of radioactivity, a combination of these three principles is used.

When outlining limits of exposure to radioactive material, numerous considerations must be borne in mind. A distinction must be made, for example, between one who is occupationally exposed to radiation and one who is not. In addition, with respect to non-occupational exposure, particularly when deliberating the possible genetic effects, it is important to know how large a segment of the population is exposed to a given level of radiation. Other variables far too numerous and complex to discuss here are brought to bear in any specific situation. Therefore, rather than delve into the myriad of rules and limits which have been promulgated by responsible authorities, it might be well to consider briefly some of the basic philosophy which has served as a foundation on which to build these principles of protection from radiation.

Perhaps the most fundamental premise on which all radiological health measures are based is that, in the absence of contrary evidence, one must assume that all radiation, of whatever type or intensity, is potentially harmful to some degree. In view of this, one might logically wonder at the advisability of pursuing any further the possible peacetime uses of nuclear energy. In fact, why not desist from any exposure to radiation at all? The obvious means of answering these hypothetical questions is, of course, to point out the utter impossibility of avoiding all exposure to radiation. Man has, from time immemorial, been exposed to radiations of varying intensities over which he has no control, radiations from the cosmic and from the natural radioactivity which has been present on our planet from the time of its inception. Admittedly, the intensity of radiations from either source is minimal. Nevertheless, since it has been present at least as long as man has inhabited the Earth, one must conclude that this unavoidable exposure to radiation must be part of the normal environment of the human race.

Acceptable Risk

To what extent, then, should we be willing to allow ourselves to be exposed to radiation in order to add to the already large number of benefits to be derived from nuclear energy? We now find ourselves face to face with the concept of the "acceptable risk." Although this term is most frequently applied to workers in the several facets of the nuclear energy field, in somewhat broader terms, it can be applied equally

well to the general population. Acceptable risk, when applied to those who are exposed to artificial, or man-made, radiation in the normal course of their employment, connotes the situation that most authorities agree exists today. The acceptable risk is defined[1] as one that is made so small that it is readily acceptable to the average individual; that is, the risk essentially is the same as is present in ordinary occupations not involving exposure to radiation. The concept of acceptable risk for occupationally exposed individuals, of course, implies that those who would work with radioactive substances or with radiation-producing devices must have sufficient training to make such an assumption valid. The Atomic Energy Commission, to the limit of its resources, has made every effort to see that only properly trained individuals gain access to radioactive substances and the machines which produce them.

Permissible Dose

The concept of acceptable risk might perhaps be looked upon as the precursor of the somewhat ambiguously-called "tolerance dose." Although this terminology has been utilized greatly in the past, in the light of current evidence, it has come to be looked upon with disfavor. Since there apparently is no threshold dose of radiation below which no harm can possibly occur, it is obviously incongruous to imply that there is a "tolerance" to the effects of radiation. A more suitable term to be used in this manner is "permissible dose," which has been defined as the dose of ionizing radiation that, in the light of present knowledge, is not expected to cause appreciable bodily injury to a person at any time during his lifetime. Limits of permissible dose have been set up for total body radiation, radiation of a specific organ, and for relatively small cross section areas for external exposure to ionizing radiation. A point that bears strong emphasis is that all permissible doses listed are *maximum* limits; it should be a matter of principle with those who work with radioactive substances or radiation-producing machines to keep all exposure or dose at the lowest possible level. In practice, it has been shown many times that it is possible to keep actual exposure to radiation to a mere fraction of the maximum permissible exposure at the point of interest.

Biological Effects of Radiation

In the course of this presentation, reference has been made to the biological effects of ionizing radiation. It might be well to consider briefly certain of these effects as well as certain theories of action which give rise to these phenomena.

Specificities in the *modus operandi* of ionizing radiation are only poorly understood. Several hypotheses have been advanced to explain the gross effect of radiation, which has been stated to be ionization. One of these, the so-called "target" theory, intimates that there are certain sensitive constituents within cells which are directly ionized by the absorption of nuclear energy.

Another, the "activated water" theory, states that the demonstrable effect is secondary to an effect on the molecules of the solvent of the tissue of interest. That is, some sort of decomposition action occurs in the liquid phase of a biological system or organ which gives rise to the effects more commonly attributed to radiation damage.

Most authorities believe that neither theory completely describes the mechanism of action of ionizing radiation; rather, a combination of these two theories and others more closely approximates the true situation.

Inherent in this ionization process which occurs in the medium with which radioactive emanations react is an absorption of energy. A statement has been made[2] regarding the relatively small amount of absorbed energy required to produce marked effects on tissue. For example, the probable temperature rise to be expected in soft tissues with a fatal radiation dose for humans of 600 roentgens would probably not exceed 0.001°C. For this dose, it can be shown that only about one atom in each 100 million atoms is ionized!

When considering the possible biological effects of a given radiation dose, it is imperative that one knows the time interval during which the dose was absorbed, for the symptoms of exposure to radiation may manifest themselves as an acute syndrome or a chronic one. There are other determinants of radiation effect, such as the total amount absorbed, the area exposed, species and individual variability, the relative sensitivity of cells and tissues, and even the general organic condition of the subject.

Certain generalizations, which have been substantiated by experimental observation, may be made with respect to the relative sensitivity of cells and tissues to radiation. In general, the more rapidly growing cells in a given tissue are most radiosensitive. Further, the tissues and cells which are least differentiated and specialized appear to be more sensitive to radiation. Listed below are certain common cells and tissues in order of decreasing radiosensitivity:[2]

1. lymphoid tissue, particularly lymphocytes,
2. immature blood cells found in bone marrow,
3. cells lining gastrointestinal tract,
4. gonads; testes more sensitive than ovaries,
5. skin, particularly that around hair follicles,
6. endothelial cells, vascular and peritoneal,
7. epithelial cells of liver and adrenal,
8. other tissues, including bone, muscle and nervous in that order.

CAUTION
RADIOACTIVE

The symptom complex resulting from exposure of the entire body to a large dose of radiation in a short period of time has been termed the acute radiation syndrome. The probable effects in man of acute radiation doses to the whole body have been tabulated below:[3]

Probable Effect	Acute Doses In Roentgens
No obvious injury	0-25
Possible blood changes; no serious injury	25-50
Blood changes, some injury, no disability	50-100
Injury, possible disability	100-200
Injury and disability certain, death possible	200-400
Fatal to 50 percent	400
Fatal	600 or more

In peacetime, the possibility of a serious acute exposure to radiation is unlikely, with the possible exceptions of gross negligence on the part of an individual working with radioactive substances or devices which produce radioactive emanations, or in the case of an untoward excursion of a nuclear reactor. Therefore, the chronic effects of radiation are probably more important to us from a health standpoint than are the acute. Chronic effects are usually directly related to dose, although if exposure is sufficient a condition resembling the acute syndrome may develop. It is important to emphasize that these chronic effects, in most cases, result from an exposure considerably in excess of the maximum permissible doses to be found in the literature. Certain of these chronic effects are carcinogenesis, genetic mutations, decreased fertility, premature aging and shortened life span, embryological anomalies, and cataract induction. Of these, probably only the genetic effects could result from less than maximum permissible exposures to radiation. As the means of detecting damage from radiation become more refined, other chronic effects may well be demonstrated and the ones just mentioned understood more clearly.

Nuclear energy and its applications undoubtedly show promise of giving to mankind countless blessings of indescribable magnitude. In fact, if properly utilized, it may well be the key to our survival in what is perhaps the most dynamic period of recorded history. Not the least of the innumerable problems to be resolved before its full benefit may be realized is a more objective outlook on the program with all of its ramifications and a less sensational, more scientifically accurate presentation to the public in general of both the attributes and the liabilities of a nuclear energy program. Professional people in all walks of life have a moral obligation to contemporary generations and succeeding ones as well to aid in this rapidly expanding field.

Dr. Edwin G. Williams, a United States Public Health Service physician, in an address presented at the In-service Training Course in Radiological Health at the University of Michigan School of Public Health in February of 1951, concluded his remarks by saying:

"The fields of atomic energy and nuclear physics will continue to modify and enrich our lives. Advances in these fields are accompanied by serious threats to our personal health and comfort and to the healthfulness of our environment. It is unacceptable that these threats will not be met and controlled by the combined efforts of science, industry, and public health."

May positive thinking of this kind never cease.

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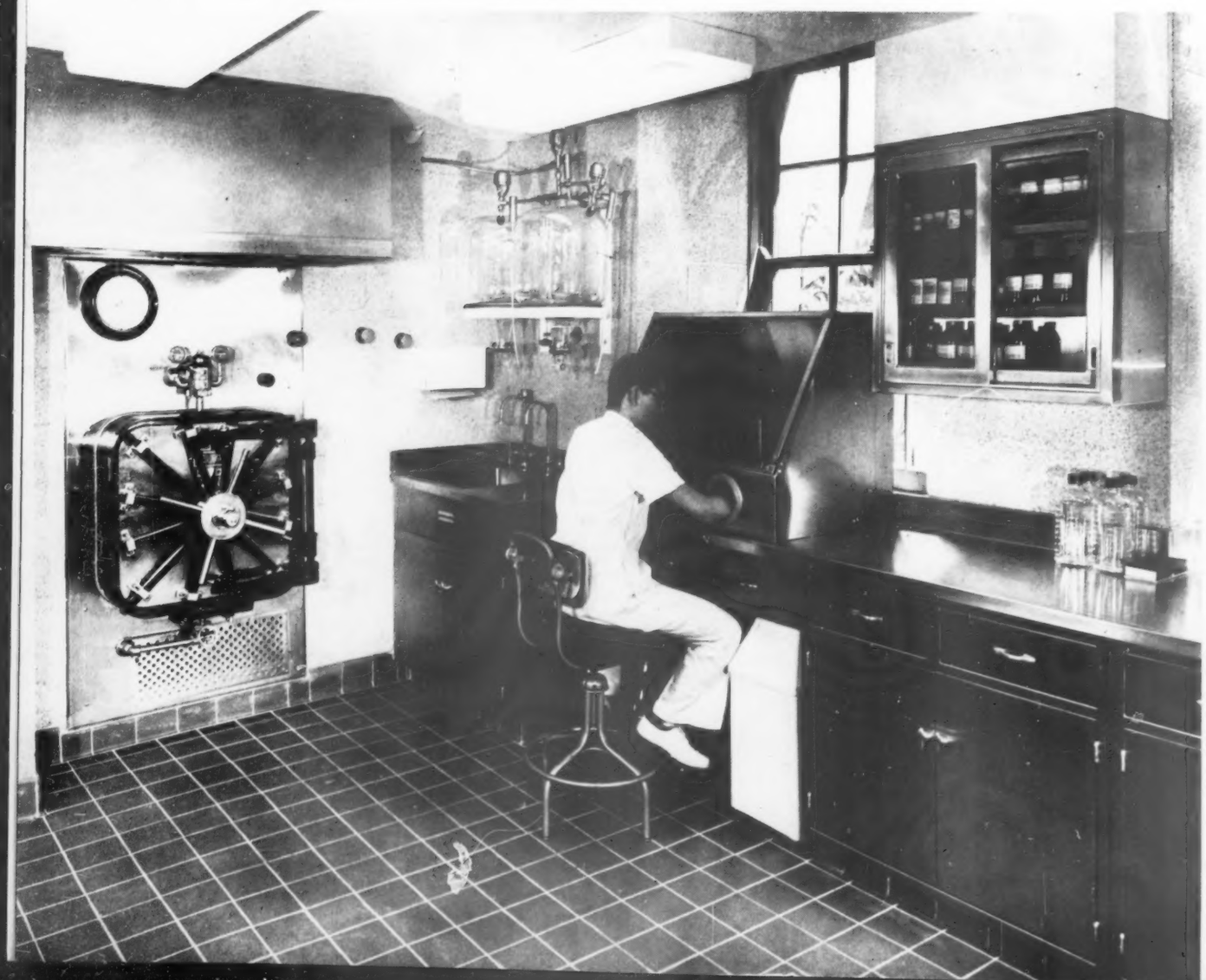
PHOTO BLACK STAR

PHARMACY SERVICE

UNIVERSITY OF CHICAGO CLINICS

by PETER SOLYOM

A view of the sterile solutions room showing aseptic filling hood



► THE UNIVERSITY OF CHICAGO CLINICS and School of Medicine are a part of the Division of Biological Sciences of the University of Chicago. The function of the Clinics is to provide facilities for the clinical departments necessary for teaching, research, and medical care. The Clinics are comprised of a group of hospitals which include Albert Merritt Billings Hospital, Bobs Roberts Memorial Hospital for Children, The Chicago Lying-In Hospital, the Home for Destitute Crippled Children, and the Argonne Cancer Research Hospital. These units have a total of about 720 beds. The Outpatient Department provides medical care for ambulatory patients. There are approximately 200,000 outpatient visits each year.

Pharmacy Organization

The Pharmacy Department is staffed by a total of 25 persons, including 16 registered pharmacists and 9 lay persons. Three of the registered pharmacists hold supervisory positions and include the Chief Pharmacist who is responsible to administration for the overall pharmacy service; the Assistant Chief Pharmacist who is responsible to the Chief Pharmacist for the proper operation of interdepartmental dispensing, manufacturing operations, and the isotope pharmacy; and the Dispensary Supervisor who is responsible to the Chief Pharmacist for the operation of the Dispensary.

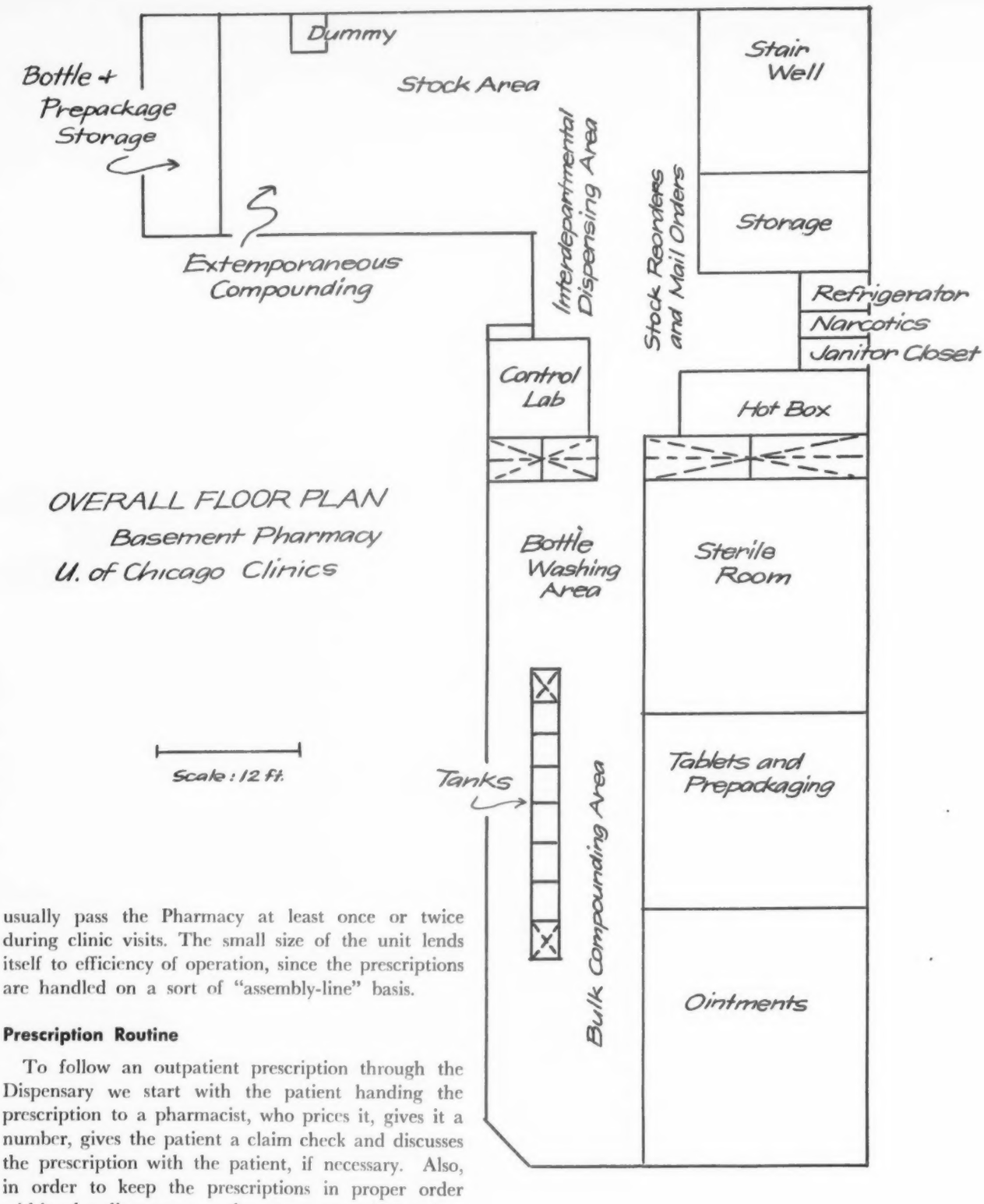
PETER SOLYOM is Chief Pharmacist of the University of Chicago Clinics, Chicago.

Dispensary

The Dispensary combines in a single operation the filling of outpatient and inpatient prescriptions. This combination works very well because the peak periods for the two types of services do not coincide and this results in a relatively even work-load throughout the day. This unit is staffed with six registered pharmacists, a typist, and a cashier under the supervision of the Dispensary Supervisor. The work-load varies between 450 and 750 prescriptions per day with an average of about 650. Sixty percent of these prescriptions are for inpatients.

The physical area of the Dispensary is relatively small. It occupies about 475 square feet of space on the first floor just off the outpatient admitting lobby. The location is an excellent one since all outpatients

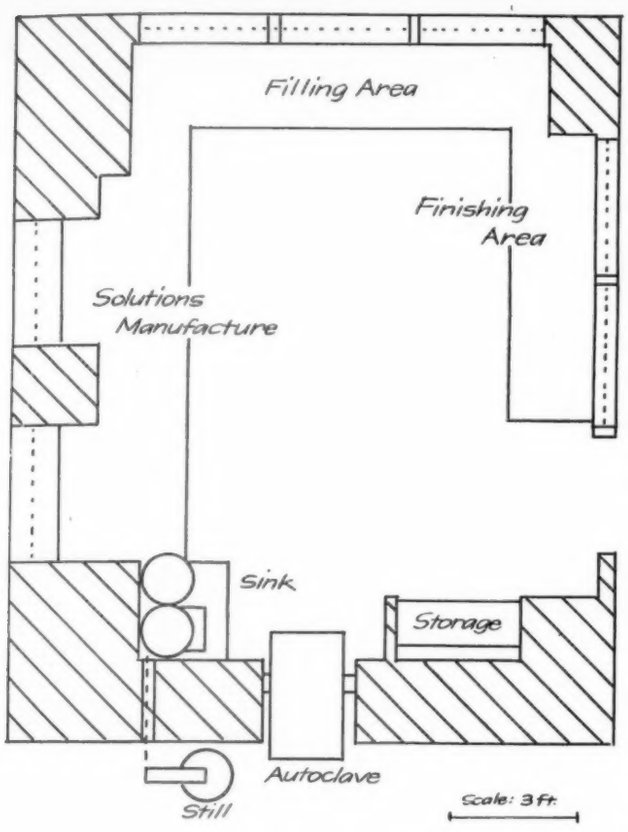
A view of the Manufacturing Unit showing the equipment for preparing ointments

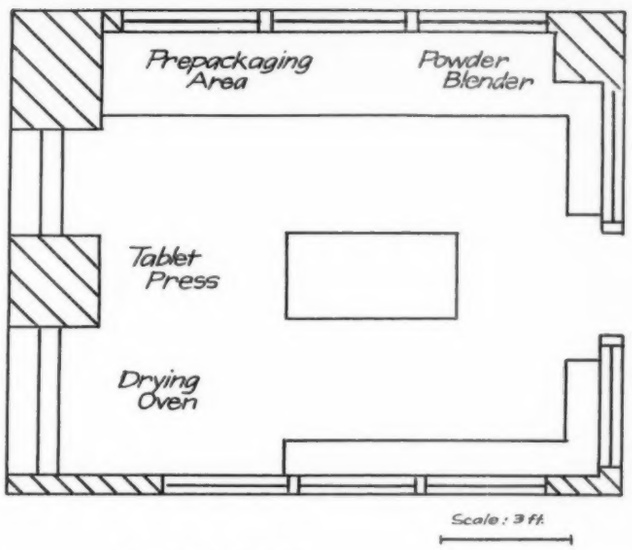


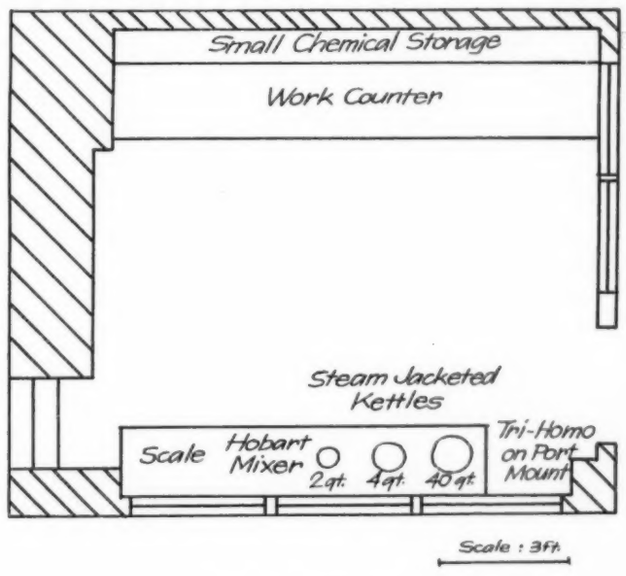
usually pass the Pharmacy at least once or twice during clinic visits. The small size of the unit lends itself to efficiency of operation, since the prescriptions are handled on a sort of "assembly-line" basis.

Prescription Routine

To follow an outpatient prescription through the Dispensary we start with the patient handing the prescription to a pharmacist, who prices it, gives it a number, gives the patient a claim check and discusses the prescription with the patient, if necessary. Also, in order to keep the prescriptions in proper order within the dispensary so that none get misplaced, a large numbered ticket with about two-inch numbers—similar to those used in stores to assure patrons of their proper turn—is clipped to the prescription. The prescription then goes to the typist who completes the label and slips it under the clip on the prescription. They are then separated into two groups depending on which side of the center counter the medications are



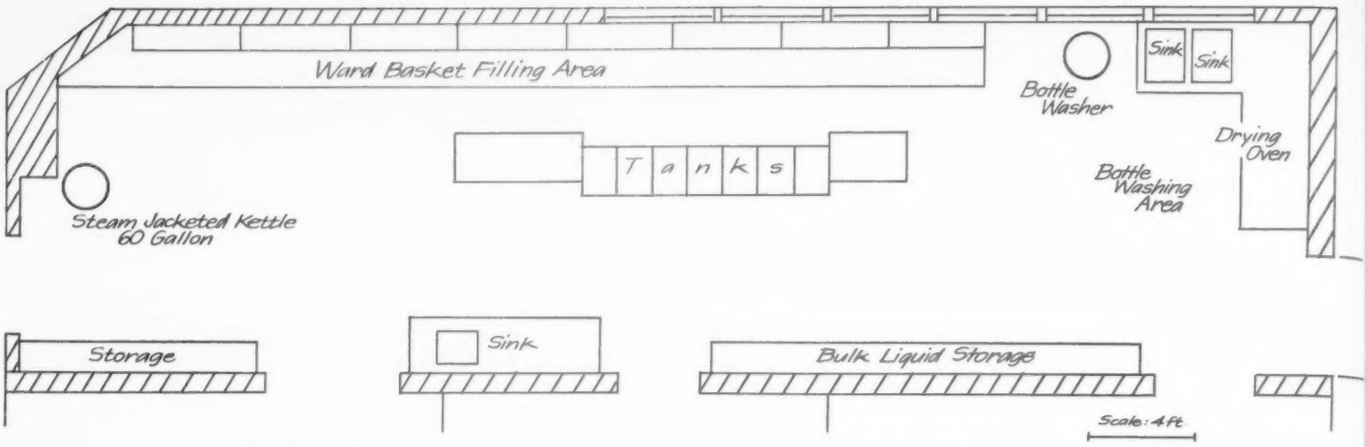




stored. The center counter contains the most frequently dispensed items in bulk or in prepackaged units. Slower moving items are stored along three walls of the Dispensary. Pharmacists then fill the prescription and affix the label to the container. It is rare that the pharmacist has to take more than three or four steps to fill a prescription and can usually fill a great number of prescriptions from one position.

The completed prescription is then forwarded to a pharmacist who devotes his time exclusively to inspecting the work previously done. He checks the prescription number, name of the patient, directions, and the physician's name. Using physical characteristics and prepackaging code labels the pharmacist also checks, as far as possible, the identity of the medication. This individual also checks and removes the large numbered ticket clipped to the prescription, keeps track of them so that none are missing, and determines the reason for any delay if the number is slow coming through. Many a misplaced prescription would have gone unnoticed if it were not for this system. The prescription is then given to the cashier to be wrapped and delivered to the patient at the same time the fee is collected.

Inpatient prescriptions are filled on the same "assembly line" basis and are sorted according to the various nursing units. These prescriptions are picked up from, and delivered to, the nursing units on a regular six times daily schedule by a lay pharmacy helper.



BULK COMPOUNDING and WARD BASKET FILLING AREA

Since the dispensary area is not large enough to include sections for compounding and storing large stocks of medication, areas for small batch compounding and for bulk storage of the medications dispensed from the upstairs units are located in the basement immediately below the Dispensary. Prescriptions requiring compounding are dropped down a mail chute connecting the basement with the upstairs and are filled by a pharmacist on duty in the compounding unit. Approximately ten percent of the total prescription volume of the department requires compounding. The finished prescription is then returned to the Dispensary via a dumbwaiter, which is also used to send stock supplies up from the storage area. The entire department is connected by an intercommunication system and supplies from the basement can be obtained in a hurry if necessary.

To avoid monotony in the Dispensary, professional personnel are on a rotating basis.

Evening pharmacy service is provided by two pharmacists who alternate on the evening shift and also do some day work. This service is available until midnight. Thereafter, until the Pharmacy opens at 8:30 A.M., service is provided by nursing supervisors.

Manufacturing

The manufacturing section was completely remodeled two years ago. Since various pharmaceutical operations interfere with each other, it was decided to separate the area into several glass partitioned rooms closed off from each other. All cabinet work is of stainless steel and glass, the floor is red clay tile which is easy to clean. The walls are done in a unique process called "Cement Enamel." This furnishes a continuous wall covering of colored glaze spray on cement.

The sterile room has facilities for the production of sterile ophthalmic solutions, small volume parenterals, and irrigating solutions. Solutions may be sterilized by heat or by bacterial filtration and filled into sterile containers under aseptic conditions. Sample products and batch sizes are 1400-30 ml. Procaine Hcl. 1 percent, 100-5 ml. Pilocarpine 2 percent Collyria, 100-1000 ml. Ringer's Solution for Irrigation, and 200-1 ml. polyethylene tubes of Fluorescein 2 percent Collyria.

The tablet and prepackaging room contains equipment for the manufacture of tablets and a counting machine for the prepackaging of tablets and capsules. Bulk powders are also packaged into dispensing containers in this room. Prepackaging work is done by a lay person under the supervision of a pharmacist.

The ointment room contains a large capacity scale, mixing equipment, and steam jacketed kettles for the manufacture of ointments. A great many types of ointments are manufactured and batch sizes vary from five pounds to four hundred pounds. A sixty-gallon steam jacketed kettle is located just outside this room and large batches of ointment are manufactured in it. The semi-fluid ointment is pumped from this kettle to an ointment mill and packaged immediately into ointment jars.

Bulk liquids are manufactured in the bulk compounding area and include such items as 25 gallons of Benedict's Qualitative Solution, 50 gallons of X-Ray Developer, 50 gallons of Hand Lotion, and 100 gallons of Mouth Wash.

Every attempt is made to manufacture in large batch sizes using nonprofessional help under the immediate supervision of a pharmacist and, where practical, to package the item immediately into the dispensing container. One hundred gallons of mouth wash in a diluted form is manufactured and immediately packaged into 1500 eight-ounce containers. Thus a month's supply of mouth wash is ready to be placed at the patients' bedside. Because of the large volume used and the storage space required, it is impractical to prepackage such items as alcohol 70

percent, soap solutions, and germicides. These solutions are made up in 80-gallon batches and stored in stainless steel tanks immediately adjacent to the ward basket filling area. These gallon goods are packaged on a day-to-day basis.

Basket Filling and Interdepartmental Dispensing

It was found convenient for both the Pharmacy and the Nursing Departments to fill ward baskets only three times weekly. The baskets are collected from the twenty-one nursing stations on Monday, Wednesday and Friday, filled and returned within two or three hours, thus providing the balance of time and personnel to large batch, assembly-line type manufacturing. This area also serves as a source of drugs and chemicals for the research and teaching laboratories of the medical school. Overall, a total of 10,000 items are dispensed per month from this area.

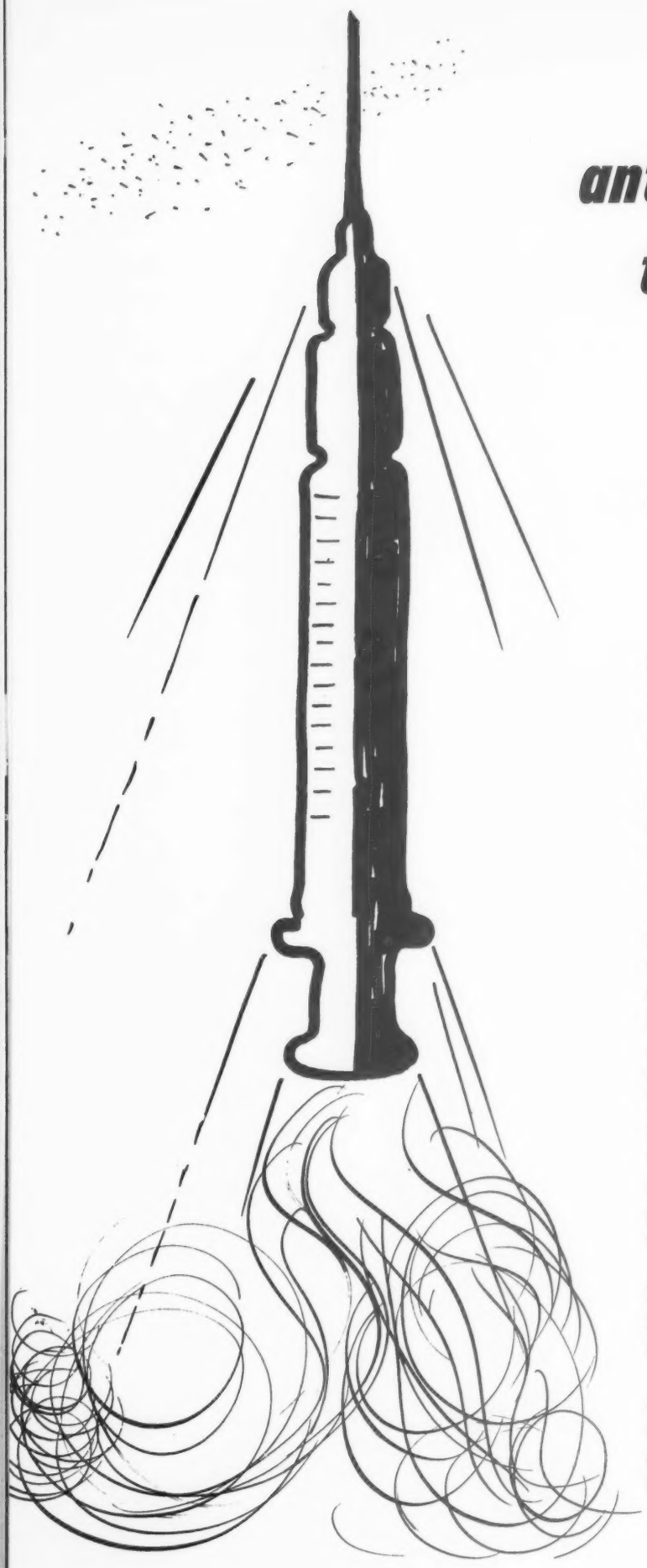
Above: Ward basket filling area of the Pharmacy at the University of Chicago Clinics. An 80-gallon mixing tank is shown at the far end. Stainless steel storage tank for fluids are to be seen at the left of the photograph

Below: Another view of the ward basket filling area showing a 60-gallon steam-jacketed kettle and a 100-gallon mixing tank

Radioisotope Pharmacy

Radioactive medications at the University of Chicago Clinics are procured and dispensed by the Pharmacy Department. Frequently used radioisotopes are stocked in the Isotope Pharmacy and dispensed as requested for patient use. The physician, upon deciding to use a radioactive medication, calls the pharmacist and gives the necessary information. The pharmacist calculates the amount of solution necessary to provide the required dosage by using a decay chart and slide rule. The required dosage is transferred from the stock container to a paper cut using a remote control pipette. The radioactive medication in the paper cup, which is placed in a lead container, is then taken to the patient for administration.

Prepackaging operations are carried out in this room of the Pharmacy Department at the University of Chicago Clinics



antibiotics today

a summary of recent developments in antibiotics reported at the recent symposium on antibiotics held in Washington, D. C.

► THE FIFTH ANNUAL SYMPOSIUM on Antibiotics, sponsored by the Food and Drug Administration in collaboration with the journals *Antibiotics and Chemotherapy* and *Antibiotic Medicine and Clinical Therapy,* was held in Washington, D. C., October 2, 3, and 4. Recent discoveries and advances in the field of antibiotics were reported by leading scientists from the United States and abroad. A total of 161 papers were presented.

Several new antibiotics, including sulfocidin, telomycin and premaricin, were reported. New uses were described for novobiocin and cycloserine. Results of studies were reported on amphotericin B, the first antibiotic to show promise in the treatment of systemic mycoses. New antibiotic preparations with a high affinity for lymphatic tissue were of special interest. Results of a nationwide survey on severe antibiotic reactions were discussed. The use of penicillinase in the treatment of penicillin reactions, the problem of resistant organisms, further studies on streptomycin pantothenate and cycloserine, and antibiotic combinations were among the topics presented.

Chairman of the Symposium was Dr. Henry Welch, Director of the Division of Antibiotics, Bureau of Biological and Physical Sciences, Food and Drug Administration.

Because hospital pharmacists are closely associated with medical practitioners, an attempt is made here to present a brief account of some of the subjects covered. This résumé is based on information released by the Food and Drug Administration.

AMPHOTERICIN B has been prepared in a new solubilized form by Bartner, Zinnes, Moe, and Kulesza of the Squibb Institute for Medical Research. A major deterrent to the parenteral administration of the potent antifungal antibiotic amphotericin B has been its extreme water insolubility. Utilizing a mixture of amphotericin B with sodium desoxycholate it has been possible to prepare a water-soluble form for intravenous administration.

The process of preparation involves suspending the amphotericin B in an aqueous solution of sodium desoxycholate, stirring until dissolution occurs, sterilizing the solution by filtration, and freeze drying. The resulting stable lyophilized powder is easily reconstituted with Water for Injection to form a clear concentrated solution which is diluted with glucose and administered by intravenous drip. The solubilization appears to be a surface active phenomenon due to the "soap like" action of sodium desoxycholate.

For amphotericin B-sodium desoxycholate solutions in mice, the oral LD_2 was greater than 330 and less than 390 mg. of amphotericin B/Kg., whereas the average intravenous LD_{50} and LD_2 values were 4.2 and 2.1 mg. amphotericin B/Kg., respectively. By the latter route the solutions were about 3 times as toxic as amphotericin B alone given as a water insoluble suspension. In rabbits, dogs and monkeys, signs of toxicity were produced by intravenous infusion of 3 to 5 mg. amphotericin B/Kg. A moderate, temporary elevation of the blood urea nitrogen was detectable in each of these three species following dosage. Only the dog exhibited a unique sensitivity i.e., hemorrhagic enteritis involving primarily the duodenum.

The use of amphotericin B in the treatment of cryptococcal meningitis was reported by Rubin, Lehan, Fitz Patrick, and Furcolow of the U. S. Public Health Service. Cryptococcal meningitis has been considered a uniformly fatal illness although the course of the disease is characterized by exacerbations and remissions. The authors reported on six cases of cryptococcal meningitis treated with intravenous amphotericin B (Fungizone, Squibb). Five of these patients are alive at the present time with follow-ups ranging from 5 to 10 months. The 6th patient was moribund at the start of amphotericin B therapy and expired after only seven days of intravenous medication.

The five living patients have received a total of 1.5 to 5.0 grams of the drug intravenously. All have shown clinical improvement, and in three this has been quite striking with the patients returning to normal activities without symptoms. Sterilization of the cerebrospinal fluid has been accomplished in all of these patients. Serial cerebrospinal fluids have shown marked improvement in cell counts and chemistries with two cases showing complete reversion to normal. Results obtained on these six patients indicate that amphotericin B is the most promising agent now available in the treatment of cryptococcal meningitis.

Results of a therapeutic evaluation of nystatin and amphotericin in oral moniliasis in infants and children were described by Huang, Sarria, and High of the Temple University School of Medicine, Philadelphia, Pa. The authors compared the therapeutic effects of nystatin, amphotericin B and a combination of amphotericin A and B in oral moniliasis of infants and children. From 1955 to 1957, 60 infants and children were treated with nystatin under various dosage regimens. Twenty-nine, or 49 percent of these patients responded promptly with marked clearing of oral lesions within 24 to 48 hours. Twenty, or 30 percent of this group showed a fairly good result and the remaining eleven patients failed to respond at all.

Since June 1956 20 infants and children were treated with 80 mg. of amphotericin B in a one ml. suspension administered topically three times a day. Prompt response was noted in seven patients (35 percent), fairly good response in eight (40 percent), and no response in the remaining five patients (28 percent).

In 1957 nine infants with oral moniliasis were treated with a suspension of amphotericin A and B containing 40 units per ml. This was swabbed on the oral cavity four times daily. Three patients in this group responded promptly to therapy, three showed a fairly good result, and three did not respond at all. Relapses were frequent in all groups of patients regardless of the agent employed therapeutically.

The results of this study indicated that nystatin, amphotericin B, and A and B are fungistatic. None of the three agents produced untoward local or systemic reactions.

ANTIBIOLYMPHINS or lymphotropic antibiotics were the subject of a paper by Malek, Kole, Herold, and Hoffman of the Institutes for Clinical and Experimental Surgery and for Antibiotic Research in Prague, Czechoslovakia. Since the lymphatic system is important in bacterial invasion, it would be desirable to have appreciable tissue concentrations of antibiotics in the lymph nodes. To this end a number of antibiotic products have been prepared with an increased affinity for the lymph system. In general, they are salts of an antibiotic base, such as streptomycin or neomycin, with polyacrylic acids, sulfonic or phosphorylated polysaccharides, or certain natural polycarboxyl acids. These macromolecular salts have been termed "antibiolymphins." Streptolymphin and neolymphin are shown to be absorbed from sites of injection primarily by the lymph system. In comparison with the antibiotic sulfates in rabbits and dogs, they yield lower but more prolonged blood concentrations, and much higher and more prolonged lymph concentrations. The acute mouse toxicities of these two antibiolymphins are much less than the ordinary sulfate salts. On intrapleural administration in dogs, neolymphin was still present in the pleural cavity after 48 hours, while neomycin disappeared in 4 hours; blood concentrations from neolymphin were low but lasted beyond 48 hours, those from neomycin reached a peak in 1 hour and disappeared in 12; lymph node concentrations were extremely high with neolymphin and lasted beyond 72 hours, those from neomycin were low and lasted only 12 hours. Intraperitoneal administration yielded similar results. The same chemical principle of tissue localization can undoubtedly be applied to other chemotherapeutic substances.

BACITRACIN ointment in the prophylaxis of ophthalmia neonatorum was reported by Anderson and Posner of Harlem Hospital, New York City. In an investigation involving 1,144 infants, bacitracin ointment (Baciguent, Upjohn), used in conjunction with mechanical cleansing of the eyes, was found an adequate prophylactic procedure against ophthalmia neonatorum.

An evaluation of bacitracin and bacitracin methylene disalicylate with carbarsone in the treatment of amebiasis was made by Alvarez of the Doctor William A. Morgan Hospital, Ciudad Trujillo, Dominican Republic. Treatment of amebiasis with the formula B1 (bacitracin, 3500 units; carbarsone, 0.25 Gm.) and the formula B2 (bacitracin methylene disalicylate, 3500 units; carbarsone, 0.25 Gm.) was studied in 64 patients: 43 hospitalized (many of them with severe dysentery) and 21 outpatients. Both types of treatment

(formulas B1 and B2) were equally effective in the treatment of amebic dysentery, although higher dosages of the B2 formula were necessary during the first days of treatment. Treatment resulted in cure of all cases of amebiasis. Absence of intolerance to both drugs was reported.

CHLORAMPHENICOL acid succinate (sodium salt) is a succinate ester of Chloromycetin. It is soluble in an aqueous solution to more than 50 percent. Payne and Hackney of Howard University and Freedmen's Hospital, Washington, D. C., reported results of animal and human investigations with this salt. On the basis of animal experiments, the increased solubility of this material promised greater clinical effectiveness when used by intramuscular injection. The increased solubility also suggested that the material might be used by nebulization in the treatment of local infections of the respiratory tract.

In human subjects, satisfactory blood levels are achieved within one hour and remain high up to the sixth hour of observation. Approximately 70 percent of a dose of 1 Gm., given intravenously, is reported excreted in 24 hours. Patients have been studied with treatment by both the intramuscular route and nebulization. Preliminary results indicate clinical effectiveness by both routes with no evidence of toxic damage by either route. The material can be injected safely with a minimum of local irritation at the site of injection.

According to Glazko, Carnes, Kazenko, Wolf, and Reutner of Parke, Davis and Co., the sodium salts of the mono- and disuccinate esters of chloramphenicol (Chloromycetin, Parke, Davis) appears to be ideal preparations for parenteral administration because of high water-solubility, minimal local irritation at the site of injection, rapid absorption, and ease of hydrolysis in the body. The monopiperazine salt of the disuccinate ester also has the same desirable properties. Both esters are readily absorbed from parenteral sites of administration, yielding therapeutic levels of chloramphenicol in the blood stream, and good urinary through-put of aryl nitro compounds. Parenteral administration of the disuccinate ester resulted in the excretion of both mono- and disuccinate esters, along with metabolic products of chloramphenicol. Oral administration of the monosuccinate ester resulted in some absorption, while very little absorption occurred with the disuccinate ester. Slow release of chloramphenicol from the ester form may be of additional therapeutic significance if hydrolysis of the ester is accelerated at the site of bacterial infections.

The use of Chloromycetin acid succinate in the treatment of acute infections was described by McCrumb, Snyder, and Hicken of th University of Maryland School of Medicine, Baltimore. Body fluid concentrations of chloramphenicol following the intravenous and intramuscular administration of this salt were determined. Peak concentrations in adults after intravenous administration appeared within 30 minutes; after intramuscular administration, within two hours. Effective levels persisted for approximately six hours following the administration of a single 1 Gm. dose. Serum levels attained and diffusion into other body fluids were equal to or better than those with other parenteral forms of chloramphenicol. Of particular importance was the observation that Chloromycetin acid succinate could be administered both intravenously and intramuscularly in much smaller volumes and with greater ease than the available parenteral preparations.

This antibiotic was employed in the therapy of several acute infectious processes including salmonella bacteremia and Rocky Mountain spotted fever. Therapeutic results comparable to those obtained previously with other forms of chloramphenicol indicate that this preparation possesses similar antimicrobial properties. In the light of these advantages it is concluded that chloramphenicol acid succinate should be employed whenever parenteral chloramphenicol is indicated.

The use of Chloromycetin acid succinate (sodium salt) in children was reported by Ross, Zaremba, and Puig of the Children's Hospital, Washington, D. C. Chloromycetin acid succinate was administered both intravenously and intramuscularly to a series of infants and children in varying single and multiple doses in order to calibrate optimal dosage in the pediatric age group. Approximately 50 infants and children with severe infections including H. influenza meningitis, septicemia, laryngeotracheobronchitis, bacterial pneumonia, salmonellosis, shigellosis, pathogenic E. coli, gastroenteritis, and typhoid fever have been treated with Chloromycetin acid succinate and the results have been generally favorable.

Pediatric experience with intravenous chloramphenicol was described by Balkcom and Kagan of the Cedars of Lebanon Hospital, Los Angeles. One hundred and three seriously ill pediatric patients were treated. The clinical response was evaluated in 85. Eighteen others were included for study of side effects and toxicity. These 18 had illnesses which could not be expected to be influenced by the drug. Of the 85 patients, 73 improved and 12 did not respond to chloramphenicol. Of the latter, 5 died. The average duration of fever after the start of intravenous chloramphenicol in the improved patients was 3 days.

Except for one patient, the side reactions and toxic manifestations were mild and transient. They were in the form of thrombophlebitis, diarrhea, skin rash, and transient granulocytopenia. The authors state that intravenous administration of chloramphenicol is practical and therapeutically effective in infections in which there are indications for the drug. It is a valuable addition in seriously ill patients until such time as the drug can be taken orally.

The combined use of gamma globulin and chloramphenicol in refractory infections was described by Knouf of the Los Angeles County Hospital and the Department of Medicine, University of Southern California School of Medicine. The author concludes that when chloramphenicol is the drug of choice in the treatment of infections it may be used for a long period of time without adverse results even in a debilitated individual. By clinical evaluation alone, there is little doubt that the effectiveness of chloramphenicol is augmented and the course of therapy shortened when adequate doses of gamma globulin are combined with the antibiotic.

Further studies on the therapeutic activity of gamma globulin-chloramphenicol combinations were described by Manning, Gagliardi, and Fisher of Parke, Davis and Co. It has been reported from these laboratories that combination treatment of mouse infections with pooled human gamma globulin and chloramphenicol provided an effect that was markedly better than additive. This was described for infections induced with strains of *Micrococcus pyogenes* var. *aureus*, *Streptococcus pyogenes*, *Proteus vulgaris*, and *Pseudomonas* sp. This report is an extension of the previous studies, using additional species of bacteria: two strains of *Salmonella typhimurium*, and one strain each of *Diplococcus pneumoniae*, *Escherichia coli*, and *Pasteurella multocida*.

Employing the method where each agent was given in doses which were deliberately subcurative, it was again found

that combined treatment with gamma globulin and chloramphenicol could be quantitated as being considerably greater than the predicted additive action. This was observed with the infections by *S. typhimurium, D. pneumoniae,* and *E. coli.* In contrast, gamma globulin given alone was inactive against infection by *P. multocida* and did not potentiate the activity of chloramphenicol.

Tests of antibiotic combinations involving chloramphenicol and oleandomycin were reported by Welch and coworkers of the Food and Drug Administration, Washington, D. C. Oleandomycin and chloramphenicol were tested in mixtures with each other and also with bacitracin, bryamycin, cycloserine, erythromycin, neomcyin, novobiocin, penicillin G, polymyxin, streptomycin, spiramycin, synnematin B, tetracycline, chlortetracycline, oxytetracycline, and vancomycin. The 16 oleandomycin mixtures were each tested against 58 test organisms and the 16 chloramphenicol mixtures were each tested against 60 test organisms. Eight genera were represented: Micrococci, Streptococci, Proteus, Pseudomonas, Salmonella, Shigella, coli, and aerogenes.

Of the 925 tests on oleandomycin mixtures, the incidence of synergism was 23.6 percent, summation 50.9 percent, no biologic interaction 22.2 percent, and antagonism 3.3 percent. Of 959 tests on chloramphenicol mixtures, the frequency of synergism was 28.1 percent, summation 39.8 percent, no interaction 27.1 percent and antagonism 5 percent. Although these results are comparable with these two series of mixtures, the chloramphenicol mixtures were more active against the gram-negative organisms, particularly against the proteus species (35.3 percent) as compared to 2.5 percent with the oleandomycin mixtures. The most predisposing factor for synergism appeared to be that the organism be sensitive to both antibiotics; this condition prevailed in cases of synergism more than twice as frequently as when the organism was resistant to one or both drugs.

CYCLOSERINE (Seromycin, Lilly) with isoniazid for use in chronic pulmonary tuberculosis was evaluated by Kirshner of the Eagleville Sanatorium, Eagleville, Pa. Fifteen patients with chronic cavitary pulmonary tuberculosis who had not responded to prolonged therapy with streptomycin, P.A.S., and isoniazid were treated with Seromycin with INH. The study comprised ten men and five women from 26 to 58 years of age. The dose of the drug was 250 mg. Seromycin wtih 150 mg. INH given twice daily.

Nine patients were able to complete six months of the therapy with no untoward effects. In six patients the drug was discontinued because of toxicity. The toxic effects were apparent clinically and early, and recurred if treatment was resumed. There was no serious toxicity and stopping the drug gave prompt relief. Laboratory studies revealed no toxic effects in any of the patients.

Toxicity included: (a) marked sedation (somnolence) in 3 patients, (b) mental depression in 3 patients, (c) mental confusion in 3 patients, and (d) rash in 1 patient.

Four patients reported an increase of well being with improvement in appetite. Four patients exhibited decreased sputum. Four patients gained a significant amount of weight (10 to 20 lbs.) There were no significant changes on x-ray and all patients remained sputum positive.

Cycloserine and isoniazid were studied by Truant and Coates of Henry Ford Hospital, Detroit, Michigan, for their effectiveness, *in vivo* and *in vitro,* on *Mycobacterium tuberculosis.* All admissions to the tuberculosis unit of the hospital were considered as possible candidates for treatment with these antituberculosis drugs if they had (a) proven pulmonary tuberculosis with a cavity of 1 centimeter or greater, (b) no previous therapy with isoniazid or cycloserine, (c) no previous history of convulsions or psychoses.

Laboratory studies, including smears and cultures for acid-fast organisms, were initiated before beginning a therapeutic regimen. Sensitivity tests using cycloserine and isoniazid were performed twice monthly on the isolates from each patient until the sputum cultures were negative. Special attention was paid to the determination of blood levels for cycloserine. A brief neurological examination was performed on each patient at weekly intervals.

The *in vitro* studies showed that cycloserine inhibited the growth of tubercle bacilli in concentrations of 10 to 80 micrograms per milliliter of medium. Approximately 20 percent of the strains were resistant to isoniazid. Combinations of cycloserine and isoniazid did not show any marked synergistic activity.

Clinical data are now available for periods of up to fourteen months. During this time, 20 percent of the patients showed side reactions consisting of fever and hyperirritability which resulted in the discontinuance of cycloserine from the therapeutic regimen. The tubercle bacilli did not develop a resistance to cycloserine during the course of therapy. There is no evidence to suspect that cycloserine will prevent the development of isoniazid-resistant strains. The investigators feel that cycloserine should be used in the treatment of selected cases, under adequate supervision.

DIHYDROSTREPTOMYCIN sulfate 80 percent and dihydrostreptomycin tripantothenate 20 percent, equivalent to 1 gm. dihydrostreptomycin base (Didrothenate, Lederle), in combination with isoniazid and/or para-aminosalicylic acid, was used in a series of 21 cases of chronic pulmonary tuberculosis by Mihaly, Thompson, Gittens, and Simmons of Harlem Hospital, New York. All patients complained of impaired hearing and had other symptoms referable to streptomycin or dihydrostreptomycin which had been previously administered. After a six-month study period, the following results were noted:

(a) All subjective symptoms (dizziness, tinnitus, headache, blurred vision, somnolence, nervousness, a heavy or drawing muscular sensation, and a generalized rash in one case) had disappeared completely. There were no relapses when medication was discontinued and no recurrences where further medication was required. Auditory acuity increased clinically in the majority of the patients.

(b) No arrested case of tuberculosis was reactivated and no active case deteriorated, by either radiological or clinical standards, on Didrothenate therapy.

(c) Sputum conversion occurred in 4 cases and sputum and gastric contents were negative for acid-fast bacilli in all patients at the conclusion of the study.

(d) No hematological aberrations were noted in 9 patients receiving complete pre-and post-treatment blood counts.

(e) Of 13 patients having pre-and post-treatment audiograms, only one showed an increased perceptive hearing loss in the second audiogram.

The authors concluded that Didrothenate is superior to the previously employed dihydrostreptomycin sulfate in the treatment of chronic pulmonary tuberculosis and further audiographic investigations were recommended.

Dihydrostreptomycin pantothenate and N-isonicotinoyl-N'-(Salicylidene) hydrazine (Salizid), in 2 gram per diem dos-

ages were administered to a group of 42 patients with fibrocavitary pulmonary tuberculosis by Katz, Donohoe, Albrite, Shutts, and Hawkins of the District of Columbia General Hospital and Walter Reed Army Medical Center, Washington, D.C. The therapeutic results appear to be similar to dihydrostreptomycin or streptomycin given twice weekly in conjunction with isoniazid or daily isoniazid-para-aminosalicylic acid. Toxicity is considerably less than previously recorded, occurring only at levels of 2 to 4 times greater than that previously encountered with dihydrostreptomycin sulfate.

ERYTHROMYCIN in the prevention of rheumatic fever was tested in a group of 52 known rheumatic subjects: 38 received 100 or 200 mg. of erythromycin daily (575 patient-months); 14 received placebos (304 patient-months). The data did not suggest protection of the patients from streptococcal or rheumatic infection. In fact, the erythromycin group included all four recurrences of rheumatic fever, all three substantial elevations in streptococcal antibody titer, and a majority of nasopharyngeal isolations of beta-hemolytic streptococci. Staphylococci resistant to erythromycin were found in throat cultures from none of the 5 patients receiving the placebo but were found in 6 of the 10 receiving erythromycin. This trial of erythromycin in the prophylaxis of rheumatic fever was made by Harris, Friedman, McLean and Tall of Children's Hospital, Philadelphia.

NOVOBIOCIN (Albamycin, Upjohn; Cathomycin, Merck Sharp & Dohme) combined with penicillin was studied by Verwey, Miller, and Baron of the Merck Institute for Therapeutic Research, Rahway, N. J., to determine the frequency of synergism, additive action, and antagonism in both *in vitro* and *in vivo* laboratory experiments. *In vitro* experiments with *Streptococcus fecalis*, *Proteus vulgaris* and antibiotic resistant and sensitive strains of *Micrococcus pyogenes* demonstrated that although both synergism and antagonism could occasionally be found, the predominating interaction was additive. Neither synergism nor antagonism when seen was particularly strong.

In vivo studies were made by Miller, Baron, and Verwey of the Merck Institute for Therapeutic Research, Rahway, N.J., to demonstrate the broadened spectrum of novobiocin-penicillin combinations. In the studies, mice were infected with a penicillin-resistant staphylococcus, a streptococcus, or a mixture of these organisms. The amount of penicillin used for therapy protected the animals against the streptococcal but not the staphylococcal nor the mixed infection; the amount of novobiocin used protected against the staphylococcal but not the streptococcal nor the mixed infection. The combination of novobiocin and penicillin protected against both the mixed and the individual infections. Such laboratory studies demonstrate the broadened spectrum of activity of novobiocin and penicillin combinations.

Novobiocin therapy in puerperal mastitis was discussed by Green and Baker of the Walter Reed Army Medical Center, Washington, D. C. During an outbreak of staphylococcal puerperal mastitis 17 cases were treated with novobiocin. Complete resolution of the inflammatory process resulted in 14 cases, and in 3 cases the process resolved to a small abscess requiring simple incision and drainage. During this period 12 cases receiving other antibacterial therapeutic agents developed massive breast abscesses requiring major drainage. Skin reaction occurred in four of the novobiocin treated cases.

An *in vitro* and *in vivo* evaluation of novobiocin and cycloserine against *Nocardia asteroides* was presented by Sanford, Hatten, and Fordtran of the Southwestern Medical School, Dallas, Texas. Nocardiosis is a chronic progressive pulmonary disease caused by *Nocardia asteroides*. Laboratory observations of the *in vitro* sensitivities of these organisms have been infrequent. A discrepancy between the effectiveness of antibacterial *in vitro* and *in vivo* has been noted. Sulfadiazine has been the most effective agent in experimental infections.

In evaluating a patient with progressive pulmonary nocardiosis, this strain of *Nocardia asteroides* was found to be sensitive *in vitro* to less than 0.08 mcg. per ml. of novobiocin. Further *in vitro* studies have been performed on six other strains of *Nocardia asteroides* against novobiocin and cycloserine using the agar plate dilution technique. Five strains were inhibited by 0.312 mcg./ml. or less of novobiocin. One strain was resistant to greater than 20 mcg./ml. of novobiocin. All seven strains were resistant to greater than 40 mcg./ml. of cycloserine *in vitro*.

Gost of the Hospital Del Ray, Madrid, Spain, reported that novobiocin appears to be a specific treatment for Malta fever and may be useful in the eradication of Malta fever in Mediterranean countries. Novobiocin (Cathomycin, Merck Sharp & Dohme) was used in the treatment of 25 cases of Malta fever when the disease was at its height and in the acute phase. The dose used was 72 to 80 capsules of 250 mg. each over a period of 15 days. During the first 5 or 6 days the clinical course of the illness is apparently not modified, the temperature remains high and the painful discomfort natural to the disease is not abated. Usually after the sixth day the temperature falls to below 37°C, although in some cases a slight rise in temperature may occur before its final disappearance. The fall in temperature is quite abrupt and with it all discomfort (articular pains, neuralgia, etc.) disappear. Some patients have been followed for as long as 9 months without relapse. Blood cultures were negative in all instances. Once treatment is begun none of the usual complications inherent to Malta fever occur (orchitis, rheumatism, etc.). In only two instances have side reactions occurred. In both an urticarial rash necessitated interruption in treatment. On renewing the treatment in these cases the urticaria promptly reappeared.

Clinical observations on the use of novobiocin in penicillin-resistant staphylococcal septicemia were discussed by Colville, Gale, and Quinn of Henry Ford Hospital, Detroit. Seven patients with staphylococcal sepsis were treated with novobiocin. The following significant features were common to all cases and preceded the onset of staphylococcal sepsis in all cases: an underlying primary disease process, hospitalization, surgical intervention, and previous exposure to various antimicrobial agents. In each instance the isolated strains of staphylococci were pigmented, hemolytic and coagulase positive. Five of the seven patients responded satisfactorily to treatment with novobiocin. Of the remaining two cases, one developed severe thrombocytopenia purpura—a previously unreported toxic reaction—on the ninth day of therapy and after receiving eighteen grams of novobiocin. In the other patient, emergence of a novobiocin-resistant strain of staphylococcus occurred after seven days of therapy.

The use of novobiocin-sulfamethiozole combination (Cathozole, Merck Sharp & Dohme) in the treatment of acute urinary tract infection was evaluated by Hughes, Coppridge, and Roberts of Durham, N. C. Novobiocin and sulfamethiozole (sufamethylthiodiazole) have been combined in a 1:3 ratio in a 500 mg. tablet with a view to reducing

the number of resistant mutants which develop under treatment and in hopes of providing a combination drug with greater antibacterial activity than each possesses alone. Twenty-five patients with acute urinary tract infections were treated with this combination drug. *In vitro* sensitivity to novobiocin was determined on all organisms isolated from patients receiving novobiocin.

Twenty-four of 25 patients treated with the combination drug were "cured." The other patient was "controlled" but the infection recurred promptly after completion of therapy. Twenty-two of 24 sulfamethiozole treated patients (controls) were "cured"; there were 2 failures. Thirteen of 14 patients treated with novobiocin (controls) alone were "cured"; there was 1 failure. Six of 39 patients receiving novobiocin developed a diffuse maculopapular rash 8 to 10 days after treatment was started.

The utility of a novobiocin-sulfamethylthiodiazole combination for the treatment of urinary tract infections was investigated by Johnson, Perry, and Sokolski of the Upjohn Co., Kalamazoo, Mich. For this purpose, some organisms ordinarily associated with such infections were developed resistant to the given drugs. A strain of each of the following species was isolated resistant to 200 mcg./ml. of novobiocin and a strain of each to 200 mcg./ml of sulfa: *Proteus vulgaris, Escherichia coli, Pseudomonas aeruginosa* and *Aerobacter aerogenes.*

The efficacy of each drug, singly and in combination, was determined with each resistant organism. The combination at 200 mcg. of each drug per ml. inhibited the growth of all eight strains of bacteria. The Albamycin-resistant strain of *Pseudomonas aeruginosa* was not sensitive to either antibiotic alone but was sensitive to the combination. At 50 mcg./ml. of each drug, all except *Ps. aeruginosa* were inhibited. However, in this case the combination was more effective than either alone.

The use of novobiocin and tetracycline phosphate in the treatment of scarlet fever was studied by Tall, Gaskill, and Coriell of the South Jersey Medical Research Foundation and Municipal Hospital, Camden, N.J. Results in this limited study indicate that not only is novobiocin inferior to tetracycline phosphate, but that it is inadequate as a therapeutic agent for the treatment of scarlet fever.

NYSTATIN (Mycostatin, Squibb) was employed by Kozinn and Taschdjian of Maimonides Hospital, Brooklyn, N.Y., in the treatment of oral thrush. Twenty cases of oral thrush in newborns and young infants were treated with daily doses of 1,600,000 units of lyophilized nystatin in aqueous suspension. The medication was given orally and by swabbing of the oral cavity every six hours between feedings. All patients improved, and 90 percent were cured after one or two courses of therapy. Therapy should be given for at least ten days, especially if surviving candida spores can be demonstrated in oral smears and cultures after an apparent clinical cure. In such cases mild relapses may occur within a week, which usually respond well to a second course of therapy. The initial response, overall cure rate, and average duration of therapy required for a cure with lyophilized nystatin compared favorably with those of other therapeutic agents and were superior to results previously obtained with non-lyophilized nystatin.

Treatment of amebic proctitis with tetracycline-nystatin was reported by Ruiloba and de Esesarte of the Hospital de Enfermedades de la Nutricion and Fierro of E. R. Squibb & Sons de Mexico. Fifteen patients with amebic proctitis were treated. Fourteen of these patients had developed the typical dysenteric syndrome. Twelve cases were considered acute and two chronic. Almost the entire group had received different antiamebic treatment previously. The diagnosis was based on proctosigmoidoscopic examination which demonstrated the existence of characteristic ulcerations, and the discovery of trophozoites of *E. histolytica* from the lesions. The whole group received tetracycline (250 mg.) and nystatin (250,000 units) in combination every 6 hours during a period of 10 consecutive days at least. Thirteen patients were cured both clinically and parasitologically.

The clinical trial of tetracycline phosphate complex combined with nystatin in the treatment of bacterial pneumonia was reported by Gallarage, Williams, and Billow of Harlem Hospital, New York. The phosphate complex salt of tetracycline combined with the antimycotic, nystatin, was used for the purpose of securing the rapid absorption and antibacterial range of the former, with the suppression of yeast-like organisms provided by the latter agent. This combination (Comycin, Upjohn) was used in the treatment of 55 adult patients with bacterial pneumonia, resulting from either pneumococcal, staphylococcal or mixed infections.

In the dosage schedule employed, two capsules at twelve hour intervals, the patients received each day tetracycline phosphate complex equivalent to 1.5 Gm. of tetracycline hydrochloride and 1,500,000 units of nystatin. The average duration of therapy was twelve days. The organisms recovered from these patients, *Pneumococcus, Beta Streptococcus, Alpha Streptococcus, Staphylococcus albus,* and *Streptococcus hemolyticus,* were all susceptible to tetracycline. The clinical response to the medication was excellent in all cases. The fever subsided to normal on the average within three days, with amelioration of clinical symptoms.

Neomycin with nystatin in the preoperative preparation of the bowel was evaluated by Hannon and Cox of Letterman Army Hospital, San Francisco. The routine preparation for colonic surgery consisted of neomycin (1 gram) plus nystatin (250,000 units) every 4 hours for 13 doses. Of 31 cases so prepared, 27 were considered successful. Four had marked vomiting and the preparation was considered inadequate.

At the time of surgery, swab cultures were taken from the bowel lumen by thoroughly soaking the swab and taking available fecal material immediately upon opening it. In the case of obstructive lesions or double-barrelled colostomies, cultures were taken both distally and proximally. The culture material was immediately placed in 2 ml. of broth and then plated on blood agar, eosin-methylene blue agar, and Sabouraud's medium, the broth was placed in thioglycollate broth and incubated. Twenty-nine of the 31 cultures were negative bacteriologically and none showed any growth of fungi. Two cultures grew moderate numbers of bacteria of the *Klebsiella-Aerogenes* group. Four patients had postoperative wound infections.

A previous series of 23 patients treated with a similar regime without the nystatin showed all cultures bacteriologically negative, but 5 showed growth of *Candida albicans.* The incidence of postoperative complications was similar in this group, and no complications due to fungi were encountered in either group.

(to be concluded in February issue)

EDWARD SPEASE -- a memorial

by CHARLES O. LEE

► EDWARD SPEASE WAS BORN at Dresden, Muskingum County, Ohio on March 31, 1883. He passed away on October 12, 1957 at the Akron City Hospital. Following a stroke last March, he recovered sufficiently to be about home until the end of the summer when he suffered a more severe one from which he never recovered.

His Experience and Education

Mr. Spease's first two years' experience as an apprentice were with John Hornung, pharmacist, Dresden, Ohio, 1901 and 1902. He entered the Ohio State University School of Pharmacy in the fall of 1903 and graduated with the Ph.C. degree in 1905 and the B.S. in 1907. He was granted an honorary Master of Pharmacy degree in 1936 by the Philadelphia College of Pharmacy and Science in recognition of his work to establish hospital pharmacy courses and to give practical training in that field of service. He became a registered pharmacist by examination in 1905. For many years thereafter he worked in a number of Ohio pharmacies during the summers and as a relief pharmacist at other times.

His Teaching Career

Upon his graduation in 1907 Mr. Spease became an Assistant in the College of Pharmacy, Ohio State University, and was advanced to the position of Assistant Professor of Pharmacy and Secretary of the College until 1916, at which time he resigned to become Dean and Professor of Pharmacy, Western Reserve University, Cleveland, Ohio. In the meantime, he was married to Alice Kelly of Pittsburgh, Pa., June 22, 1911.

Pharmacy Committee in Hospitals Organized

An outstanding contribution to the progress of professional pharmacy was made by Edward Spease during his 24 years as Dean of Pharmacy at Western Reserve University. He was Directing Pharmacist of University Hospitals of Cleveland 1932 to 1940. Through his efforts a written agreement was made between Western Reserve University and the University Hospitals of Cleveland whereby the Professor of Pharmacy in the University became Directing Pharmacist of the Hospitals, and the pharmacists in the hospitals were elected to the Pharmacy School faculty.

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To aid in carrying out this program, a Pharmacy Committee was organized consisting of the Directing Pharmacist and one representative from each of the departments of Medicine, Surgery, Pediatrics, and Obstetrics and Gynecology. The Chief Pharmacist was the Secretary of this Committee. The Committee was in charge of all medications and professional supplies and created a Drug Policy and a Professional Stores Policy. It also made it possible for pharmacy interns to reside with the medical interns. Through the cooperation of the Pharmacy Committee, Dean Spease gave the first graduate instruction in hospital pharmacy. This made him a member of the Graduate School Faculty of Western Reserve University, 1937 to 1940. In 1940 there were 13 graduate students in hospital pharmacy at Western Reserve. Furthermore, undergraduate instruction in hospital pharmacy was given to all students in the junior year and to a chosen list of senior students. During this period, articles of cooperation between the Academy of Pharmacy and the Academy of Medicine of Cleveland were agreed on, printed, and circulated. He may well be called the Father of Hospital Pharmacy.

Offices and Memberships Held

Dean Spease was president of the American Association of Colleges of Pharmacy, 1927 to 1928; a member of the National Pharmacy Week Committee, 1936 to 1939; one time Secretary, Editor, and President of the Phi Delta Chi Fraternity, and honorary member of Kappa Psi, and Rho Chi. He was a life member of the American Pharmaceutical Association and the Ohio State Pharmaceutical Association. In 1920-1921 he was chairman of the Section on Education and Legislation of the American Pharmaceutical Association, and served for many years as chairman of the legislative committee of the Ohio State Pharmaceutial Association. He was joint author of the Ohio Prerequisite Law. He was, for a time, a Fellow in the A.A.A.S.; and held membership in the American Chemical Society and the American Public Health Association. He was an associate member of the Cleveland Academy of Medicine, associate member of the Cleveland Medical Library, honorary member of the Northern Ohio Druggists' Association, member of the Cleveland Academy of Pharmacy and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. He received the Harvey

Edward Spease

A. K. Whitney Award in 1952. He was also a member of the Ohio and the Cleveland Societies, and third vice president of the United States Pharmacopoeial Convention, 1930 to 1940. He was also listed in *Who's Who in America,* volume 14, 1926-1927 and later editions, and at one time in *American Men of Science.*

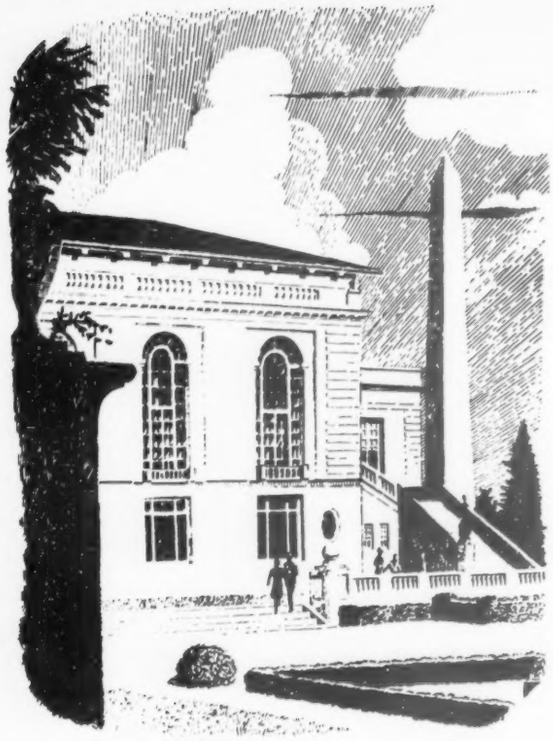
Publications

Dean Spease was co-author of "Minimum Standards for Hospital Pharmacies," adopted by the American College of Surgeons in 1936. He was author of *Pharmaceutical Mathematics,* published by McGraw-Hill Book Company, and one time chairman of a committee that planned the publication of pharmacy text books, and a co-author of the chapter on Hospital Pharmacy in *Remington's Practice of Pharmacy,* Eighth Edition.

In 1940 Mr. Spease resigned his position as Dean of Pharmacy at Western Reserve University and served as Director of Public Relations, National Association of Retail Druggists from 1940 to 1944. He then retired to Ravenna, Ohio, and continued for a time to be the Science and Prescription Editor of the *N.A.R.D. Journal.* Later he moved to a three acre lot outside of Hudson, Ohio, where he and Mrs. Spease lived in retirement. There he enjoyed his yard, trees, and garden. He also kept alert to things pharmaceutic until the fatal illness overtook him.

Those of us who knew Edward Spease well, admired him for the forthright character that he was; a man of unquestionable integrity. The pharmaceutical profession will always be indebted to him for his earnest labors and unselfish efforts to improve its educational program and to make pharmaceutical services a cooperative and a necessary feature of the health professions. This is exemplified in the pioneering work he did in the organization of a successful hospital pharmacy program at Western Reserve University, an educational program developed as a cooperative effort involving both pharmacy and medicine.

Mr. Spease is survived by his wife and a brother. Mrs. Spease continues to reside at their home at 12 John Clarke Lane, Hudson, Ohio. Memorial services were held for Mr. Spease in Christ Church Episcopal in Hudson at 2 P.M. on Saturday, October 19, 1957.



Section on Hospital Pharmacy

FOURTH PAN-AMERICAN CONGRESS

On Pharmacy and Biochemistry

► HOSPITAL PHARMACISTS representing countries from throughout the Western Hemisphere participated in the Section on Hospital Pharmacy of the Fourth Pan-American Congress of Pharmacy and Biochemistry. Meetings were held at the Hotel Mayflower in Washington, D. C., November 3-9. The Section on Hospital Pharmacy was one of several sections devoted to the various specialties within the profession. The total Congress was made up of 463 pharmacists from Latin America and an additional 125 guests and observers, making a total of 588 foreign Congress members. A total of approximately 1200 people registered at the Congress.

The Section on Hospital Pharmacy, under the leadership of Chairman Dr. Margarita Tamargo from Havana, Cuba, and Secretary Grover C. Bowles from Memphis, Tennessee, held two outstanding sessions with an opportunity to exchange viewpoints regarding practices in different countries. Seventeen papers were presented, abstracts of which accompany this article. Simultaneous interpreting services were utilized throughout the meetings. Also, help from several of our Spanish speaking friends aided in the exchange of information. Of particular note were those who, because of their ability to speak both English and Spanish, served as a link between the two groups. Special mention should be made of the help given by the Chairman, Dr. Tamargo and by Dr. Jose Gonzalez, a member of the Washington Staff of the American Hospital Association. Dr. Gonzalez also brought greetings from the A.H.A. at the opening session of the Section on Hospital Pharmacy.

Mr. Leo F. Godley, President of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, served as head of the U. S. Delegation of hospital pharmacists. He also brought greetings at the opening session on behalf of the ASHP and hospital pharmacists of the United States.

At the close of the Congress, numerous delegates expressed appreciation for the excellent facilities and hospitality shown by the host country. Special recognition was paid by the Argentinian delegation to Leo F. Godley, President; Gloria N. Francke, Secretary, AMERICAN SOCIETY OF HOSPITAL PHARMACISTS; Paul Parker, Director, Division of Hospital Pharmacy, American Pharmaceutical Association; Margarita Tamargo S., Chairman, and Grover C. Bowles, Jr., Secretary, of the Section on Hospital Pharmacy.

The Fourth Pan-American Congress was a unique opportunity for all those who participated and hospital pharmacists in the U. S. as well as foreign countries are appreciative of the very fine manner in which the Congress was organized.

Abstracts of the papers presented in the Section on Hospital Pharmacy are printed below.

Some Significant Facets of the Audit of Pharmaceutical Service in Hospitals by Don E. Francke and Clifton J. Latiolais, Ann Arbor, Mich., U.S.A.

The background, over-all objectives, and significance of the Audit of Pharmaceutical Service in Hospitals are presented. A discussion of preliminary data on certain facets of the Audit includes some aspects of the formulary system, the professional services rendered by pharmacists in hospitals, the attitudes of hospital pharmacists toward the need for a professional degree of doctor of pharmacy, and staffing patterns in different type of hospitals.

Functions and Character of Social Pharmacy by Geronimo Alfredo Cogorno, Buenos Aires, Argentina.

Not including private pharmacies, pharmaceutical assistance is given in hospitals (official and private), social assistance institutions (mutual, union, cooperatives, etc.). Thus, there can be no objection to this social service, but the following stipulations must be observed: (1) pharmaceutical dispensaries must operate according to existing laws and be staffed by licensed personnel; (2) assistance should be restricted to patients of these social institutions; (3) continuity of service must be provided; (4) medicines are to be supplied gratis or at net cost.

The conditions are justified, despite recognition of the services rendered by this assistance, in order to strengthen the stability of the private pharmacy, seriously damaged by the growth of systems distorting the legitimate and altruistic social assistance.

Needs for Hospital Pharmacists in the United States of America—1957 Through 1970 by George F. Archambault, Washington, D.C., U.S.A.

The Bureau of Census estimates the population of this country at more than 209 million in 1970. At current rates, the Nation will have added some 390,000 beds to its hospital structure in the next 13 years. In 1970, the Nation will have, if these estimates materialize, some two million beds in service.

From the latest 1956 American Hospital Association statistics, it would appear that from 500 to 600 full-time pharmacists will be closer to the actual true annual replacement needs of hospitals. Concerning replacement, it will be noted that the study predicts that 108 pharmacists will be required annually for the expected 30,000 bed growth of the hospital structure of the Nation in addition to 6 percent replacement factor of the annual hospital pharmacist working population. It is predicted that the number of full-time hospital pharmacists will be (based on 4,437 in 1955 and other factors): 4,545 in 1956, 4,761 in 1958; 4,977 in 1960; 5,193 in 1962; 5,409 in 1964; 5,625 in 1966; 5,841 in 1968; and 6,057 in 1970. The numbers of new pharmacists needed annually for replacement (on a replacement factor of 6 percent) for the years mentioned are: 273 in 1956; 286 in 1958; 299 in 1960; 312 in 1962; 325 in 1964; 338 in 1966; 351 in 1968; and 364 in 1970. To these numbers must be added 108 additional pharmacists to staff the 30,000 new beds expected to be constructed annually.

The opening session of the Section on Hospital Pharmacy, Mr. Paul Parker speaking.

A Plenary Session of the Pan-American Congress. Voting delegates of the Pan-American countries occupy front seats

Practical Suppository Formulations for Hospital Pharmacies by Robert E. Lawson, Springfield, Ohio, U.S.A.

This paper and accompanying formulas describe several (5) different types of water-soluble suppository bases and combinations in which they may be used. The formulas presented are intended to be used as a guide for the hospital pharmacist who is interested in formulating suppositories for use within the hospital and its outpatient clinics. All material presented has received exhaustive evaluation by the author at the University of Maryland and at Fitzsimons Army Hospital. This paper is based in part on a portion of a thesis submitted by R. E. Lawson to the graduate school of the University of Maryland in partial fulfillment of the requirements for the degree of Master of Science.

Sterilization of Colloidal Oatmeal for Use as a Dusting Powder for Surgical Gloves by Louis P. Jeffrey and Albert M. White, Albany, New York, New York, U.S.A.

The value of colloidal oatmeal in the treatment of acute and chronic dermatoses is pointed out and the use of this material to overcome eczema resulting from wearing rubber gloves is discussed. Problems encountered in the sterilization of colloidal oatmeal are discussed and the method of choice is described.

Mr. Grover C. Bowles, Jr., Secretary, with Miss Margarita Tamargo, Chairman of the Section on Hospital Pharmacy.

The Feasibility of a Hospital Pharmacy to Prepare Disposal-Unit Injectable Medication for the Nursing Units by Ivan F. Bourn, Herbert L. Flack, and E. R. Browneller, Philadelphia, Pa., U.S.A.

Pharmacy service in the modern hospital has many possibilities for expansion as a *service* unit within the hospital. The authors feel that one method of expanding service could be in preparation of disposable-unit injection medication.

The advantages of having an instantly available sterile injection unit, ready for administration, represent an important step forward in providing better patient care. The authors review these advantages, and present several disadvantages. This includes a cost-breakdown of the conventional method of injection versus the disposable-unit method or closed system.

One significant disadvantage at the moment is the narrow spectrum of medication that is presently available in disposable-unit injectable form. Many hospitals have not adopted the closed system because of this narrow range of products available.

The authors explore the problems and possibilities in the preparation of disposable-unit injectable medication in the hospital pharmacy that is equipped with a sterile products laboratory, or similar aseptic area, and that can obtain certain basic equipment for manufacture of small-volume sterile products.

Hypodermic Syringes and High Frequency Sound by H. M. Beal and D. M. Skauen, Storrs, Connecticut, U.S.A.

For some time high frequency sound has been employed as an excellent technic for cleaning small metal parts. Recently manufacturers have indicated that ultrasound is a valuable tool for cleaning contaminated surgical instruments.

This research was conducted to determine the value of high frequency sound as a means of both freeing and cleaning frozen hypodermic syringes.

Evidence is presented to show that a large percent of those syringes which cannot be freed by conventional means may be removed after ultrasonic insonation. Experiments were conducted to determine the extent to which high frequency sound cleaning compares with routine cleaning of hypodermic syringes.

Radioactive Pharmaceuticals—A New Challenge to Hospital Pharmacists by Clifton J. Latiolais, Ann Arbor, Mich., U.S.A.

The expanding utilization of radioactive isotopes in medicine has created an increased demand for technically trained personnel. The hospital pharmacist is challenged with the responsibility of contributing his services in handling radioactive pharmaceuticals. To do so, he needs specialized training and there are numerous opportunities available for obtaining such training. The significant contributions which the hospital pharmacist can make to the hospital's radioisotope program are elucidated.

Utilizing Information Sources in Hospital Pharmacy Practice by Gloria N. Francke, Ann Arbor, Mich., U.S.A.

Sources of information helpful to the practicing hospital pharmacist are presented. Particular attention is given to utilization of relatively new references and texts, as well as material which might be of special interest to pharmacists from the Pan-American countries. Mimeographed material supplemented the paper.

Hospital Pharmacy Representation in National Hospital Associations by Joseph A. Oddis, Chicago, Ill., U.S.A.

The advantages of having pharmacy representation in national associations are evident. This provides for close liaison with hospital administrators through avenues such as private correspondence, publications in hospital journals and personal contact at hospital gatherings. Other measures include the development of educational programs, sound legislation, raising of standards and adoption of policy statements at the national level pertaining to hospital matters.

The Outpatient Pharmacy as an In Vivo Prescription Laboratory for Pharmacy Students, by Harold J. Hamilton, Louise Pope and William Heller, Little Rock, Ark., U.S.A.

The desirability and methods of providing more "practical" experience in dispensing by Schools of Pharmacy have often been discussed by educators. A syllabus for a course in Prescription Practice as conducted in the outpatient pharmacy of the University of Arkansas Medical Center is presented. Certain problems are pointed out. These include: simulating the retail environment; pricing of prescriptions; the use of the Formulary System; need for adequate supervision and supervisors.

Some Criteria for Establishing Minimum Standards for Pharmacy Practice in Hospitals by Paul F. Parker, Washington, D.C., U.S.A.

The paper discusses some principles to serve as a basis for the development of standards of pharmacy practice in hospitals. The principles are applicable both in the initial establishment of such standards and in adaptation to meet the constantly changing pattern of medical care.

A General and Technical Study of the Pharmaceutical Organization of a Hospital, Taking into Consideration the Isolated Position of a Pharmacy and its Relation to the Rest of the Services Rendered by a Hospital by Sebastiao Soares do Nascimento, Recife, Pernambuco, Brazil.

The author explains, particularly, the organization and performance of the pharmacy of the "Conjunto Sanatorial Otavio de Freitas," a hospital for pulmonary diseases, where the author is chief of the Service of Pharmaceutical Assistance.

Problems in Hospital Pharmacy in Canada Today by I. E. Stauffer, M. Connon, P. Takenaka, and J. F. Moir. Presented by Love Chabak, Toronto, Canada.

Three major problems confront hospital pharmacists in Canada. First is an acute shortage of hospital pharmacists with specialized training. Second, the practice of pharmacy in hospitals is not covered by some provincial Pharmacy Acts. The third problem relates to the growing interest in hospital insurance and prepayment schemes.

The majority of hospital pharmacists believe that the best line of defence will be obtained in working through established pharmaceutical associations, and in 1955 the Canadian Society of Hospital Pharmacists was granted representation on the Council of the Canadian Pharmaceutical Association. Courses in hospital pharmacy administration are now being offered in several colleges, scholarships and fellowships in this specialty are becoming more numerous, and institutes and refresher courses are conducted. Studies are being made of Provincial Pharmacy Acts and problems pertaining to institutions of less than 100 beds are being investigated. Future developments, such as the establishment of a national pharmacy examining board and the formation of a Canadian Commission on the Accrediation of Hospitals, are being viewed with interest. It is hoped that the Canadian Society of Hospital Pharmacists may have a voice in areas which pertain to hospital pharmacy.

Hospital Pharmacy Service in the 'Seguro Social of Costa Rica by Rafael Angel Montero G., San Jose, Costa Rica.

There are 20 hospitals in Costa Rica to serve the population of more than one million. To protect the social welfare of the Costa Rican citizens, the "Social Seguro" benefits were established by national law in 1943. Two groups of services were provided: (A) accident insurance, life insurance and pensions, and (B) illness and maternity medical care. Part B benefits are financed equally by the employee, employer and the nation. Total payments are seven and one-half percent of the monthly salary up to and including a salary of 400 colones per month (about $50.00). The employer pays only two and one-half percent. The two principal hospitals in San Jóse are the San Juan de Dios and the Seguro Social. The former is an 1800 bed charity hospital.

The Seguro Social hospital in San Jóse has 400 beds and here is located the central pharmacy which serves a network of 19 other hospitals and clinics with manufactured and prepackaged items. Over 600,000 prescriptions are filled annually. The Seguro Social hospitals are operated under the formulary system and a printed formulary has been prepared and is revised frequently by the Pharmacy and Therapeutics Committee.

Plans are now underway to reorganize and modernize the pharmacy service of the Seguro Social chain of hospitals.

Hospital Pharmacy in France by Marcel H. Guillot, Paris, France.

Dr. Guillot spoke extemporaneously and discussed pharmacy service in French hospitals and the education and training of the French hospital pharmacists, pointing out that internships have been established in France for more than a century.

Contribution of the Colombian College of Pharmacy to the University Hospital of Cali by Alcides Narvaez Reyes, Cali, Colombia.

The abstract for this presentation was not available.

Therapeutic Trends

edited by WILLIAM JOHNSON

Compound IS-499—A Long-Acting Inhibitor of Gastric Secretion

IS-499, (1-methyl-2-pyrrolidyl) methyl benzilate methyl methosulfate, is a substance which has atropine-like properties. Twenty-four oral doses of IS-499 varying between 5 and 20 mg. were given to five normal subjects, and the salivary flow was measured from collections with a dental aspirator. Doses of 10 mg. taken by mouth partly inhibited salivary flow after a latent period of two hours, but the maximal effect was not reached until about four hours after taking the drug. The reduction in salivary flow lasted from seven to nine hours. The unusually long duration of action of IS-499 was encouraging and the feature which prompted testing the effect of this drug on gastric secretion. Results of tests in seven normal subjects and in five patients with peptic ulcer are presented. Clinical trials of this drug, which in low doses by mouth has a selective action of long duration on the gastric secretion of acid, are now being undertaken with a view to controlling secretion of acid in patients with duodenal ulceration. The results of this study by Douthwaite *et al* are presented in the *Brit. Med. J.* 2:275 (Aug. 3) 1957.

Compound 217-MI—Treatment of Glaucoma

Recently there has become available a tertiary and a quaternary form of an extremely potent thiophosphate anticholinesterase agent. The quaternary form (217-MI) is 2-diethoxyphosphinylthioethyl-trimethyl-ammonium iodide. With the evidence that the quaternary agent is a potent anticholinesterase agent that does not permeate the blood-brain barrier and therefore has no central effects, the investigation of the miotic and antiglaucomatous effects of this drug in the human eye was begun. The quaternary form of the thiophosphate termed 217-MI is a white crystalline water-soluble compound. In *A.M.A. Arch. Ophth.* 58:363 (Sept.) 1957, Leopold *et al* report that 217-MI controlled intraocular pressure previously uncontrolled by the combined therapy of other miotics and acetazolamide. It controlled intraocular pressure previously controlled by other miotics, but the dosage and frequency of administration were greatly reduced. The duration of action of 217-MI is longer than that of any commonly used miotic and therefore may be useful in dampening the diurnal fluctuation. The 0.25 percent and 0.1 percent concentrations of 217-MI solution in isotonic saline are stable indefinitely at 5°C. and show slow diminution in activity at room temperature. Some side effects were observed, but there were no obvious systemic effects following the ocular administration of 217-MI. The drug for this study was supplied by Campbell Pharmaceutical Co.

9-alpha-Bromo-11-Ketoprogesterone—Progestational Activity

9a-Bromo-11-ketoprogesterone is an orally effective substance with definite progestational activity. Considering individual differences in reaction, it may be assumed that the threshold dosage is approximately 60 mg. daily for a period of 15 days after proliferation by means of estrogen. In dosage of 80 mg. to 100 mg. 9a-bromo-11-ketoprogesterone daily, characteristic secretory changes in the endometrium were rather uniformly observed. Vaginal smears showed changes as are usually observed during luteal phases of the normal menstrual cycle, after administration of daily dosages of 100 mg. or more of the drug. There were practically no regressive changes after daily administration of 60 mg. of the drug, and a rise of basal body temperature was observed after the daily administration of 80 mg. or more of 9a-bromo-11-ketoprogesterone. This drug exhibits greater progestational activity than the generally used oral anhydrohydroxyprogesterone. This study is reported by Wied and Davis in *Obst. Gyn.* 10:411 (Oct.) 1957. The 9a-bromo-11-ketoprogesterone was supplied for this study by the Squibb Institute for Medical Research as Braxorone.

Aluminum Powder—For Thermal Burns

In the majority of centers in which relatively large numbers of thermal burns are treated, the exposure method has supplanted the occlusive dressing method as the treatment of choice for the local burn wound. Aluminum powder with a mean particle size of 50 microns formed a very satisfactory cover on the burn surface. It should be free from lead and other injurious metals and it is sterilized by baking in dry heat for two hours at 320° F. In *A.M.A. Arch. Ind. Health* 16:414 (Nov.) 1957, Maxem describes a method in which aluminum powder is used in the treatment of thermal burns. He reports that aluminum powder produces astringent coating effects comparable to

tannic acid when applied locally to the acute thermal burn. The resulting eschar is tough and pliable and tends to bend rather than break, and so splinting, traction, and suspension are not necessary. Circumferential burns can be handled with ease.

Desacetylmethylcolchicine—In Gouty Arthritis

Demecolcine (desacetylmethylcolchicine) is one of a number of alkaloids which have been isolated from the plant *Colchicum autumnale,* which also is the source of colchicine. Numerous studies of the pharmacological effects of this drug in animals have been reported and it has been used in the treatment of patients with chronic myelogenous leukemia and other neoplastic diseases. Because of the similarity of demecolcine and colchicine, Colsky *et al* have observed its effect in the treatment of patients with acute gouty arthritis and report their findings in *A.M.A. Arch. Int. Med.* 100:765 (Nov.) 1957. They report that demecolcine causes rapid symptomatic and objective improvement in patients with acute gouty arthritis and rarely produces undesirable gastrointestinal reactions, such as those seen after colchicine ingestion. This drug has potent bone-marrow-depressing activity, and pancytopenia was produced in two patients treated with frequent courses of this drug. These patients also developed generalized loss of hair on the scalp, face, and body. When therapy was discontinued in both instances there was return to normal of the peripheral blood elements. Regrowth of hair also occurred after a period of several weeks. This drug should not be used for chronic maintenance therapy and these workers suggest that further study of other colchicine derivatives be made. The Ciba Pharmaceutical Products, Inc. supplied the demecolcine used in this study as Colcemide.

Dithiazanine—An Orally Effective Trichuricide

Whipworm infections were completely eliminated in 87.5 percent of patients who were treated orally with a dosage schedule of 200 mg. dithiazanine three times a day for five days. The cure rate was 71 percent when a dosage schedule of 200 mg. twice a day was employed. The anthelmintic spectrum of this drug also includes activity against *Ascaris lumbricoides.* The observation that this compound is active against these two species of nematodes is significant since they coexist frequently in the same host. The results of this study by Frye *et al* as reported in *Am. J. Trop. Med.* 6:890 (Sept.) 1957, indicate that this compound is a very effective trichuricide which is suitable for oral administration. Dithiazanine (3-3″ diethylthiadicarbocyanine iodide) for this study was supplied by Eli Lilly and Co.

Acetazolamide—In Sickle-Cell Disease

Evidence has been produced to show that acetazolamide inhibits the occurrence of sickling of red cells *in vitro* and *in vivo.* It is suggested that the drug exerts this effect by inhibiting the action of the enzyme carbonic anhydrase. The enzyme is concerned with the reduction of the hemoglobin. The abnormal hemoglobin S in patients with sickle-cell disease undergoes molecular rearrangement during the process of reduction to form long slender rods which alter the shape of the red cell. At the present time there is no effective treatment for sickle-cell disease, and it is suggested that acetazolamide may be employed to control the occurrence of sickling. A report by Hilkovitz in the *Brit. Med. J.* 2:266 (Aug. 3) 1957 indicates that preliminary experiments have shown the ability of acetazolamide to inhibit the sickling phenomenon *in vitro* when mixed with blood from a patient with sickle-cell disease. The effect was also noticeable when the drug was administered to the patient, it then being seen that the occurrence of sickling was inhibited *in vitro* as well as in circulating venous blood. A therapeutic trial is in progress and the results so far are encouraging.

Quinidine—A Long-Acting Preparation

Quinidine has been used successfully in the treatment and prevention of various cardiac arrhythmias, particularly extrasystoles, paroxysmal tachycardia, atrial fibrillation, and flutter. Multiple daily and nightly doses are often necessary to maintain an effective plasma level. In order to avoid multiple doses, attempts have been made at various times to administer a slower and longer acting preparation. Bellet *et al* report on the use of a long-acting quinidine gluconate tablet, in a small series of patients, in *A.M.A. Arch. Int. Med.* 100:750 (Nov.) 1957. Dosage schedules and results are outlined and it is suggested by these workers that further clinical trials be made in order to establish more definitely the clinical usefulness of this preparation. Dur-Tab Quinidine Gluconate (S.M., sustained medication) was prepared for this study by the Wynn Pharmacal Co.

Ethiquinium Chloride—IN 292

Ethiquinium Chloride (IN 292), an asymmetric bisquaternary ammonium salt, appeared to be an effective hypotensive agent according to a report in the *New England J. Med.* 257:971. In the study described, ethiquinium was used orally in the treatment of a "pilot group" of ambulatory patients with arterial hypertension for periods up to sixteen months of continuous therapy.

The ethiquinium chloride for clinical use was supplied by Irwin, Neisler and Company, Decatur, Illinois

Timely Drugs

Alertonic

COMPOSITION: Each 45 ml. or 3 tablespoonsfuls contain 2 mg. pipradrol (Meratran) hydrochloride, 10 mg. thiamine hydrochloride, 5 mg. riboflavin, 1 mg. pyridoxine hydrochloride, 50 mg. niacinamide, 100 mg. choline, 100 mg. inositol, 1 mg. iodine as potassium iodine, 100 mg. calcium glycerophosphate, minerals, and 15 percent alcohol.

INDICATIONS: Functional fatigue, mood depression, nutritional deficiency.

SIDE EFFECTS AND CONTRAINDICATIONS: Contraindicated in agitated pre-psychotic patients, paranoia, or other cases where hyperexcitability, anxiety, chorea or obsessive-compulsive states are present.

DOSAGE: One tablespoonful 3 times daily, 30 minutes before meals.

PACKAGING: Bottles of 16 ounces.

SUPPLIERS: Wm. S. Merrell Company.

Cathozole

COMPOSITION: Tablets containing 125 mg. sodium novobiocin (Cathomycin) and 375 mg. sulfamethylthiadiazole.

INDICATIONS: Infections of urinary tract, acute and chronic uncomplicated and resistant; ureteritis, urethritis, prostatitis, pyelonephritis, and pyelitis of pregnancy; infections associated with trauma, foreign bodies or instrumentation.

SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally sensitivity reactions; possible overgrowth of nonsusceptible organisms due to use of antibiotics; white blood cell counts should be performed during administration.

DOSAGE: Adults, 2 tablets 3 or 4 times daily; children, 2 to 8 tablets daily in divided doses.

PACKAGING: Bottles of 24 and 100.

SUPPLIER: Merck Sharp & Dohme.

Clysmathane

COMPOSITION: Single use, disposable rectal unit of 37 ml. containing 0.625 Gm. theophylline monoethanolamine (Theamin).

INDICATIONS: Bronchial asthma and acute left ventricular failure.

SIDE EFFECTS AND CONTRAINDICATIONS: None.

DOSAGE: One unit administered as a retention enema before retiring.

PACKAGING: 37 ml. disposable rectal unit with prelubricated rectal tube.

SUPPLIER: C. B. Fleet Company, Inc.

Combid

COMPOSITION: Sustained release capsules (Spansules) containing 5 mg. Darbid and 10 mg. Compazine.

INDICATIONS: Control of physical and psychic components of ulcer and other gastrointestinal disorders.

SIDE EFFECTS AND CONTRAINDICATIONS: Should not be administered to patients with glaucoma, pyloric obstruction, or prostatic hypertrophy; should not be used where nausea and vomiting are believed to be manifestation of intestinal obstruction.

DOSAGE: One capsule every 12 hours.

PACKAGING: Bottles of 30.

SUPPLIER: Smith, Kline & French Laboratories.

Compazine Spansule

COMPOSITION: Sustained release capsule containing 10 mg. or 15 mg. proclorperazine (Compazine).

INDICATIONS: Mental and emotional disturbances, nausea and vomiting.

SIDE EFFECTS AND CONTRAINDICATIONS: Minimal side effects; contraindicated in comatose or greatly depressed states due to central nervous system depressants.

DOSAGE: 10 or 15 mg. upon arising, may be repeated in late afternoon or evening for round-the-clock protection; for "morning sickness' of pregnancy, 10 or 15 mg. before retiring.

PACKAGING: Bottles of 30 and 250 capsules.

SUPPLIER: Smith, Kline & French Laboratories.

Darbid

COMPOSITION: Sugar-coated, pink, tablets containing 5 mg. Darbid (isopropamide) iodide.

INDICATIONS: Anticholinergic for adjunctive management of ulcer and other gastrointestinal disorders, providing continuous 24-hour therapy with one tablet.

SIDE EFFECTS AND CONTRAINDICATIONS: Some reports of dry mouth, blurred vision, and urinary retention; should not be used in patients with glaucoma, pyloric obstruction, or prostatic hypertrophy.

DOSAGE: 5 mg. every 12 hours, usually with adjuvant measures such as diet, antacids, sedatives, rest and psychotherapy.

PACKAGING: Bottles of 50.

SUPPLIER: Smith, Kline & French Laboratories.

Enovid

COMPOSITION: Scored tablet containing 10 mg. norethynodrel with 0.15 mg. ethynylestradiol 3-methyl ether.

INDICATIONS: Primary and secondary amenorrhea, menorrhagia, metrorrhagia, oligomenorrhea, inadequate luteal phase, dysmenorrhea, and premenstrual tension.

SIDE EFFECTS: Nausea may be encountered, and daily dose may be cut in half or given in divided doses for 3 days, then returned to regular dose; intermenstrual spotting, usually evidence of inadequate dosage; following discontinuance of treatment, intermenstrual interval of first untreated cycle is commonly prolonged for approximately one week.

DOSAGE: Usually 10 mg. daily, in accordance with dosage guide for condition being treated.

PACKAGING: Bottles of 50 tablets.

SUPPLIER: G. D. Searle & Company.

Leritine

COMPOSITION: Tablets containing 25 mg. Leritine (anileridine) dihydrochloride; 2 ml. ampuls and 30 ml. vials containing 25 mg. per ml. (narcotic).

INDICATIONS: Analgesic for relief of pain and related symptoms associated with extensive burns, fractures,

carcinoma, angina pectoris, renal colic, biliary colic, acute congestive heart failure, infection, surgery, dental procedures.

SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally vomiting and nausea; possible respiratory depression with intravenous administration; possibility of addiction.

DOSAGE: Orally, 25 mg., repeated every 6 hours if necessary; subcutaneous and intramuscular injection, 25 to 50 mg. for adults, repeated every 4 to 6 hours if necessary; intravenous, in support of anesthesia, 50 to 100 mg. added to 500 ml. 5% dextrose in water, and 5 to 10 mg. injected slowly followed by amount desired at a relatively slow drip. Caution: The sudden injection of more than 10 mg. may produce apnea.

PACKAGING: Tablets, bottles of 100 and 500; injection, packages of 1 and 25 ampuls of 2 ml. and single 30 ml. vials.

SUPPLIER: Merck Sharp & Dohme.

Nebs

COMPOSITION: Tablet containing 0.3 Gm. (5 gr.) acetyl-p-aminophenol (APAP).

INDICATIONS: Tension headaches, neuralgia, muscular aches and pains, dysmenorrhea, bursitis, lumbago, sciatica, arthritis, and rheumatism.

DOSAGE: Usually one tablet every 4 to 6 hours; limit is three doses in any 24-hour period.

PACKAGING: Bottles of 30 tablets.

SUPPLIER: Norwich Pharmaceutical Company.

Panalba

COMPOSITION: Capsule containing tetracycline (Panmycin) phosphate complex equivalent to 250 mg. tetracycline hydrochloride and 125 mg. novobiocin (Albamycin) sodium.

INDICATIONS: Primarily in mixed infections in which invading organisms are more susceptible to the combination than to either antibiotic alone; particularly effective against strains of *Micrococcus aureus, Streptococcus fecalis,* and *Proteus vulgaris.*

DOSAGE: One or two capsules 3 or 4 times daily.

PACKAGING: Bottles of 16 and 100 capsules.

SUPPLIER: Upjohn Company.

Panmycin KM

COMPOSITION: Syrup containing in each ml. 25 mg. tetracycline as equivalent of hydrochloride, 20 mg. potassium metaphosphate, and preservatives.

INDICATIONS: Same as for other tetracycline (Panmycin) products.

DOSAGE: For adults, 10 ml. every 6 hours or 20 ml. every 12 hours; for children, 10 mg. per pound of body weight with total daily dose given in either 4 or 2 equally divided doses.

PACKAGING: Bottles of 2 and 16 ounces.

SUPPLIER: Upjohn Company.

Pathibamate

COMPOSITION: Tablet containing 400 mg. meprobamate and 25 mg. tridihexethyl iodide (Pathilon).

INDICATIONS: Duodenal ulcer, gastric ulcer, intestinal colic, spastic and irritable colon, ileitis, esophageal spasm, anxiety neurosis with gastrointestinal symptoms, and gastric hypermotility.

SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally, drowsiness or vertigo; contraindicated in glaucoma, pyloric obstruction, and obstruction of the urinary bladder neck.

DOSAGE: One tablet 3 times a day at mealtime, and 2 tablets at bedtime.

PACKAGING: Bottles of 100 and 1,000 tablets.

SUPPLIER: Lederle Laboratories.

Polymagma

COMPOSITION: Each 30 ml. contain 300 mg. dihydrostreptomycin base (as sulfate), 120,000 units polymyxin B sulfate, 3 Gm. Claysorb (activated attapulgite), 270 mg. pectin, with parabens, in a special alumina gel.

INDICATIONS: Symptomatic treatment of diarrhea, and specific therapy in diarrheas due either to streptomycin or polymyxin-sensitive organisms.

SIDE EFFECTS AND CONTRAINDICATIONS: Constipation may occur with overdosage; overgrowth of nonsusceptible organisms may result from use of antibiotics over a period of time.

DOSAGE: 20 ml. (4 teaspoonfuls) 3 or 4 times daily before meals. For infants and young children, suggested initial dose, 2 teaspoonfuls 3 times daily.

PACKAGING: Bottles of 8 ounces.

SUPPLIER: Wyeth Laboratories.

Robaxin

COMPOSITION: Scored tablets containing 0.5 Gm. of 3-(o-methoxyphenoxy)-2-hydroxypropyl-1-carbamate (methocarbamol).

INDICATIONS: Skeletal muscle relaxant.

SIDE EFFECTS AND CONTRAINDICATIONS: Minor side effects such as light-headedness, dizziness, nausea rarely.

DOSAGE: 4 Gm. initially for adults, may be increased to maximal daily dose of 9 Gm.

PACKAGING: Bottles of 50 and 500.

SUPPLIER: A. H. Robbins Co., Inc.

Spontin

COMPOSITION: Ristocetin A.

INDICATIONS: Treatment of gram-positive bacterial infections; effective against wide range of staphylococcal, streptococcal, and pneumonococcal infection.

SIDE EFFECTS: Occasionally, skin rash, diarrhea and thrombophlebitis; irritating if deposited in extravascular tissues.

DOSAGE: For pneumococcal or streptococcal infections, 25 mg. per Kg. per day intravenously; for majority of staphylococcal infections, 25 to 50 mg. per Kg. per day; daily dosage should be divided into two or three equal parts administered at 8 or 12-hour intervals.

PACKAGING: Sterile, lyophilized powder in vials representing 0.5 Gm. ristocetin A activity.

SUPPLIER: Abbott Laboratories.

Tricofuron Improved Vaginal Suppositories and Powder

COMPOSITION: Each vaginal suppository contains 0.25 percent furazolidone (Furoxone) and 0.375 percent nifuroxime (Micofur) in a water-miscible base which melts at body temperature; the powder contains Furoxone 0.1 percent and Micofur 0.525 percent in a powder base composed of dextrose, lactose, citric acid, and cornstarch.

INDICATIONS: Specific trichomonacide; for trichomoniasis and vaginal moniliasis.

CONTRAINDICATIONS AND SIDE EFFECTS: Occasional local sensitivity or irritation.

PACKAGING: Suppository of 3 Gm., hermetically sealed in green foil, in box of 12; powder in plastic insufflator of 15 Gm. with 3 disposable tips, and glass bottle of 30 Gm.

SUPPLIER: Eaton Laboratories.

Consulting WITH BOWLES

GROVER C. BOWLES JR., *Baptist Memorial Hospital, Memphis, Tennessee*

►Is it necessary to have a Class 3 as well as Class 4 and 5 Narcotic Tax Stamp to fill outpatient and inpatient narcotic prescriptions?

Yes. Class 4 is the authority to administer narcotics. Class 5 is the authority to deal in "Exempt" narcotics and Class 3 is for retail dealers and is required for hospitals filling outpatient prescriptions.

Further information regarding the purchase, utilization and accounting for narcotics may be found in THE BULLETIN OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, Volume 14, May-June, 1957, pages 295 and 318-325.

►Should the various milk companies be allowed to hold displays in the hospital?

If hospital policy permits displays to be held by the pharmaceutical representatives, then I see no objection to displays sponsored by the various milk companies, publishers of medical text books, surgical instrument companies, and other groups who regularly contact the medical staff.

►Please recommend a convenient method of cleaning catheters that may be suggested to outpatients using Solution G.

Perhaps the simplest method of cleaning catheters used for irrigating the urinary bladder is as follows: Rinse the catheter with cold tap water immediately after removal, wash thoroughly with warm water and soap, paying particular attention to the lumen of the catheter. Rinse again with cold water and allow to air dry. When dry, roll in a clean towel or cleansing tissue ready for the next use

Catheters of this type are usually made of rubber and may lose some of their elasticity on repeated use and washing. Some elasticity may be restored to the catheter by allowing it to soak in a weak vinegar solution (one tablespoonful to a quart of cold water) for a few hours following the usual cleaning procedure. The catheter is then rinsed in cold water and dried in the usual manner.

Lubricating jelly should be used to lubricate rubber catheters and contact with mineral and vegetable oils should be avoided. Contact with cresols, phenols, terpenes, organic solvents, and chlorinated hydrocarbons should be avoided.

►Should prescriptions for outpatients be filled in the hospital pharmacy?

The Guide to the Application of the Minimum Standard for Pharmacies in Hospitals, 1950 Revision, states, "Only those orders and prescriptions originating within the hospital should be filled by the hospital pharmacy. Prescriptions written by physicians who are not members of the hospital staff should not be filled by the hospital pharmacy. Regulations pertaining to the dispensing of medications to hospital personnel should be formulated and enforced."

As a matter of policy, most hospitals do not permit the filling of prescriptions for people off-the-street in the hospital pharmacy.

►How can a pharmacy intern practice pharmacy in the hospital when, more often than not, he is working in a state other than the one in which he is registered?

Ordinarily, state license is not required for the pharmacy intern because he is practicing under the direct supervision of a pharmacist registered in the state. Some questions may arise as to the legality of the pharmacy intern taking night calls and working week-ends without the direct supervision of a registered pharmacist. Questions involving such situations should be referred to the State Board of Pharmacy for clarification.

►Who should determine the brand of a product to purchase? Pharmacy Committee, Pharmacist, Purchasing Agent, Administrator, Other?

The pharmacist is legally and morally responsible for the drugs dispensed from the pharmacy. Therefore, the purchase of pharmaceuticals is properly the responsibility of the pharmacist.

Experts in hospital management have usually agreed that the pharmacist is the only member of the hospital staff with the background and ability to purchase drugs intelligently and well.

The late Dr. Malcolm MacEachern had this to say in his textbook, "Hospital Organization and Management":

"The purchase of drugs and pharmaceuticals is a specialty which can be carried out to best advantage by a pharmacist trained in managing a hospital pharmacy and under the control of the administrative office. It is therefore not advisable to have the purchasing for pharmacy done by a general purchasing agent."

The Minimum Standard For Pharmacies in Hospitals states in Section 5 that "the pharmacist in charge shall be responsible for specifications both as to quality and source for the purchase of all drugs, chemicals, antibiotics, biologicals and pharmaceutical preparations used in the treatment of patients."

Book Reviews

► **SUBSIDIA PHARMACEUTICA. Published by the Scientific Center of the Swiss Pharmaceutical Association, Zurich, 1957. 220 pages, price 45 Swiss francs.**

These pharmaceutical Supplements have been published by the Swiss Pharmaceutical Association to assist the practicing pharmacist in maintaining current knowledge and information about new drug products, brand names, etc. The book, partly in French and partly in German, is published in loose-leaf form to which new supplements can be added conveniently.

The first section, Index Nominum, presents a list of those new drugs which have been given names by the World Health Organization. In addition, the list mentions the names adopted by the principal pharmacopeias. It is the plan of the Editors to add to this list continuously and to include other names such as those used in *New and Nonofficial Drugs*. The second section of the book is devoted to a discussion of the pharmacological actions of drugs. While only one category of drugs is discussed in the book at the present time, it is the intent of the Editors that additional material will be presented from time to time for insertion into this section of Subsidia Pharmaceutica. At present there is a general discussion (in German) of the pharmacology of the autonomic nervous system. This is followed by a section specifically concerned with the sympathomimetic agents. The pharmacological activities of the different therapeutic agents are treated in a concise, yet complete, manner.

The remaining sections, dealing with such matters as assay methods for new drugs, pharmaceutical apparatus, lists of formulas, tables, etc., have only been well started. However, additions to these various chapters will be prepared on a continuing basis.

It is still too early to predict the extent of the value of this book to practicing pharmacists. However, if it is continued in the same manner as it has been started, it will without doubt become an important supplement to the existing pharmaopeias. It should also prove to be a valuable reference tool for pharmaceutical laboratories, teachers of pharmacy, etc. Subsidia Pharmaceutica represents a good example of an effort by a national pharmaceutical association to provide a continuing source of authorative and unbiased information to its members and to other pharmacists who may wish to obtain it.

The book is published partly in German and partly in French.

J. WOUTER HUISMAN

► **NEW ENGLAND HOSPITALS, 1790-1833. By Leonard K. Eaton. Published by the University of Michigan Press, Ann Arbor. 1957. 6" x 9¼", 282 pages, Illustrations. Price $6.00.**

Although many histories of individual hospitals have been published in this country and abroad, there still remains a great need for general historical works dealing with the development of the hospital as a social institution. A significant attempt to fill this gap has been made by Professor Eaton in his regional study of early New England hospitals. In general, the author's effort "to place the hospital in its total culture perspective" is accomplished with skill and insight.

The tradition which led to the founding of a number of institutions for the sick in Massachusetts and Connecticut. between 1790 and 1833 is described by the author as "creative conservatism." One may or may not accept this designation, but it is interesting to note, as Eaton points out, that these early voluntary hospitals received substantial state support and grants without succumbing to state control.

In 1790, there were comparatively few inhabitants of New England who had actually seen a hospital. By 1833, where Eaton's narrative ends, a number of important hospitals and mental institutions such as The Massachusetts General Hospital, The Boston Lying-In Hospital, the Hartford Retreat and The New Haven General Hospital had come into existence. From the impressive bibliographical essay and notes at the end of the work, it is evident that the writer has painstakingly examined primary sources such as institutional and official archives, personal papers, minutes of hospital committees and reports of trustees, correspondence, clinical records, and related documents. The result is an authoritative and well-written account of the beginnings, character, financial and administrative problems, as well as the teaching and research which prevailed in these early New England institutions. Being a professor of architecture as well as a social historian, Dr. Eaton was eminently qualified to write the chapter in the book dealing with early hospital architecture in the United States. Here the reader will find a very informative discussion of the work of such pioneer American architects as Bullfinch and Parris; their contributions to hospital construction are compared with hospital architecture in Europe of that period and the author's verdict is that American hospitals were then generally superior to those on the continent. Since Bullfinch and Parris were, in Eaton's words, "never faced with the responsibilities of remodeling ancient structures like the Hotel Dieu or La Charite, [They] could plan from the ground up."

Like the prominent historian of medicine, Richard H. Shryock, Eaton tends to overemphasize the short-term influence of Louis' numerical method (medical statistics) on therapeutics in the United States during the first half of the nineteenth century. This reviewer believes that a number of other factors were at least as important in overthrowing the general bloodletting, calomel pushing and blistering so rampant before the Civil War.

Dr. Eaton's work can be read with profit by pharmacists, physicians, hospital administrators, historians, and others who are interested in the growth of the hospital in American society.

ALEX BERMAN

► **GATHERCOAL AND WIRTH PHARMACOGNOSY. By Edward P. Claus, Ph.D. Third Edition, 731 pages 10¼" x 7", 306 Illustrations and 1 Color Plate. Lea & Febiger, Publishers, Philadelphia, Pa. Price $12.50.**

The most noteworthy change in this edition is the emphasis on the chemical, rather than the taxonomical classification. This, in my opinion, fills a great need—with special reference to the "Newer Drugs" and "Prescription Specialties." There is, however, a condensed Taxonomical Classification in Appendix I of the more im-

portant drugs from both the animal and plant kingdoms, accompanied by a list of the chemicals and commercial products derived from these.

The biological origin of plant and animal drugs is highlighted; the macroscopic and microscopic descriptions of the more important drugs are retained. A second, new, and beneficial, feature is the addition of a Key for the Identification of Powdered Drugs (Appendix II). This serves as a most useful and helpful guide. Appendix III discusses the Cultivation of Drug Plants and is supplemented with some beautiful photographs—one, of which pictures a test field of first year plants of *Hyoscyamus niger* and another a test field of first year plants of *Digitalis purpurea*.

Four new chapters have been added—Antibiotics, Immunizing Biological Products, Allergens and Allergenic Products, and Pesticides. Under Antibiotics the historical background is discussed and the commercial production of antibiotics is highlighted with excellent photographs. A table giving all the antibiotics recognized in the U.S.P.XV and N.F.X is supplied. A monograph, similar to that of other plant drugs is given for each antibiotic including the title, synonym, definition, descriptions, tests, uses and dose. Both official and trade marked products are considered; also, structural formulas are furnished. Some unofficial antibiotics are considered as well as those undergoing clinical trial. The table (page 596) listing the antibiotics official in the U.S.P.XV and N.F.X gives a classified list i.e. those derived from Molds, Bacteria and from Soil Actinomycetes.

This text is written in accord with the U.S.P.XV and N.F.X, and supplies information regarding the first year that the official drug was recognized and the year it was deleted, or whether it is official to date. Many trademarked products are treated as a separate part of the official monograph. The latest material on the modern therapeutic drugs such as Rauwolfia, Reserpine, Streptodornase, Streptokinase and Hyaluronidase is introduced. ACTH, Cortisone Acetate, and Deslanoside are among others discussed.

The contents of this remarkable text form 17 Chapters: (Chapter 1) A General Introduction. This defines the Scope of Pharmacognosy, Official and Unofficial Drugs, Evaluation of Drugs (Organoleptic, Microscopic, Biological, Chemical and Physical) Chromatographic Study and Analysis of Vegetable and Animal Drugs. A wealth of necessary and valuable information characterizes this chapter. Under Microscopic Evaluation of Drugs will be found two excellent photographs—one depicting Microfiltration, the other (Fig. 2) Microsublimation. (2) The Chemical Classification of Drugs and The Chemistry of Drugs. Different Classes of Drugs, with their chemical composition, and examples of each are given. (3) Carbohydrates—discusses the definition and furnishes examples of the various kinds. (4) Glycosides—Gives the definition and describes about 12 different classes. A table of the ones official in the U.S.P.XV and N.F.X is given; ones not official, but used, are also considered. Structural formulas are given for many. Some exquisite photographs and drawings of the cellular elements help to make this subject outstanding. (5) Tannins. (6) Fixed Oils and Fats, Waxes—official, and unofficial ones are discussed with photos and drawings of histological elements to enhance the descriptions. (7) Volatile Oils, Alcohol Oils, and Aldehyde-Volatile Oils. Both classes are treated at length and examples of official ones given. (8) Resins, Oleoresins, Gum. (9) Alkaloids—10 different classes are discussed and many examples of the official ones are illustrated with structural formulas. A number of rare photographs of the plants containing these alkaloids help make this chapter very impressive. (10) Endocrine Products—Drugs derived from the Pancreas, Pituitary, Parathyroid, Thyroid, Adrenals, Gonads and from the Liver and Stomach. (11) Vitamins and Vitamin Containing Drugs. (12) Enzymes and Enzyme Containing Drugs. (13) Proteins and Related Substances. (14) Antibiotics. (15) Immunizing Biologicals. (16) Allergens and Allergenic Preparations. (17) Pesticides.

The last four new chapters added to this third edition by Dr. Claus will no doubt constitute the ones of greatest interest to the practicing pharmacist since they discuss drugs which are frequently called for on prescriptions. They are described at length in the text but will not be discussed in this review; space will not permit.

As one reads through this magnificent work on pharmacognosy he cannot help but be impressed with thoughts of gratitude toward God, the Divine Author of all nature, who, in His munificence toward His creatures, has created these drugs of plant and animal origin for the benefit of all mankind.

This work should be the one of choice for both students, and graduates of Pharmacy; I believe it to be without a peer—as a work of its kind. It would prove a valuable addition to the library of any practicing pharmacist as both a reference book, and as a "refresher course" in the subject of pharmacognosy.

SISTER MARY OSWALDA, I.H.M.

► **QUANTITATIVE PHARMACEUTICAL CHEMISTRY, Fifth Edition. By Glenn L. Jenkins, John E. Christian, and George P. Hager. Published by McGraw-Hill Book Company, New York, 1957. 552 pages. Price $8.50.**

The numerous changes in the official methods of analysis, described in the U.S.P. XV and the N.F. X. are incorporated in this new edition of *Quantitative Pharmaceutical Chemistry*. According to the authors in their preface, the primary object of the book is "to furnish students of pharmacy with a systematic course covering the quantitative chemical and physical methods, official in the *United States Pharmacopeia* and the *National Formulary*, through the selection and explanation of typical procedures."

The authors have sought to "classify the large number of official procedures according to type methods of analysis for effective and convenient instruction." They intend the book "for use in didactic instruction and also as a laboratory manual." However, in using it as a textbook, it will be necessary to supplement the theoretical parts in order to make understandable to the students the "knowhow" of many of the analytical principles used. In reading the part on titrations in non-aqueous solvents for instance, one can't help feeling that too much was sacrificed in order to "avoid expansion of the book to unwieldy size by inclusion of detail of subject matter that is readily available in general reference." Although a list of General References appears on the first pages of the book, it seems to be a pity that those references are not mentioned at the places where they are needed as a supplemental source of information.

The content of the book is arranged in three parts: Part I treats of general methods of gravimetrical and volumetric analysis; Part II contains the special methods of pharmaceutical analysis, such as alkaloidal assaying, analysis of volatile oils and enzymatic assays; Part III treats of physiochemical methods and instrumental techniques.

Completely new are the chapters on Chromatography (for the assay of Oral Trisulfapyrimidines Suspension) and on Radioactivity (for the assay of Sodium Radio-iodide Solution). New problems and questions and many new illustrations have been added.

Summarizing, the book is a good laboratory manual for students, and is also valuable for the more skilled analyst, who wants to orientate himself in this special field.

J. WOUTER HUISMAN

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

edited by CLIFTON J. LATIOLAIS *and* LEO F. GODLEY

BACTERIOSTATS, LOSSES FROM INJECTIONS

Losses of Bacteriostats from Injections in Rubber Closed Containers, Royce, A. and Sykes, G., Pharm. J. 179:172 (Sept. 7) 1957

Rubber closed injections containing bacteriostats lose substantial quantities of bacteriostats on storage due to simple absorption by rubber and to diffusion through rubber. The work of the authors shows that the British Pharmacopoeia's method for equilibrating rubber with bacteriostatic solutions through pre-treatment is not adequate. Allowing for a short time-lag for diffusion to take place within the rubber, retreatment with bacteriostatic solutions resulted in considerable further uptake. In addition, the B.P. does not take into account the fact that a partitioning of a bacteriostat between two immiscible solvents, water and rubber, is involved. Various bacteriostats have widely different partition ratios.

Equilibration of rubber components ensures a safe concentration of the bacteriostat in an injection upon storage for a few months. During longer storage periods, diffusion losses are inevitable and the concentration of the bacteriostat is progressively reduced. Losses depend on such factors as type, thickness, surface area of the rubber, volatility and concentration of the bacteriostat employed, and volume of solution in the container. Diffusion losses can be reduced by various means, such as, by a paraffin wax seal on the outer surface of the rubber closure. Phenol and benzyl alcohol were the most promising agents examined; while the phenylmercuric salts were absorbed by rubber to the greatest extent, suggesting that they are not suitable bacteriostats for rubber closed containers.

The authors conclude that there is no complete answer to the problem of loss of bacteriostats from injections. However, a suitable seal combined with prior equilibration of the rubber component might serve as a practical solution. Also, losses can be reduced by careful selection of bacteriostat and rubber closure.

CLIFTON J. LATIOLAIS

QUALITY OF TABLETS

Sulphonamide Tablets, A Survey, Bagnall, H. H. and Stock, F. G., Pharm. J. 179:336 (Oct. 26) 1957.

In this survey, the authors analyzed 200 samples of different sulfa tablets from 30 different manufacturers, together with five samples of uncertain origin. Analyses were made on the quantitative content and tablet disintegration time to determine whether these samples met the British Pharmacopoeia requirements. Of the 200 samples, 31 failed to meet either one or both of these test requirements. Of these 31 failures, ten were due to quantitative content; twelve failed to pass the disintegration test. Three samples had incorrect composition in addition to incorrect strength. Four samples failed both disintegration and uniformity tests, and two failed both these tests plus insufficient amounts of the named drugs.

This is the third group of drugs analyzed by the authors. The first group—barbiturate tablets—presents manufacturing problems related to their physical properties and the second group—penicillin tablets—related the problem of chemical deterioration. Sulfa drugs do not normally suffer from either of these problems and the authors further expound the thesis that the quality of tablets serves as an indicator of the extent of experience and skill of manufacturers. In this study 23 complaints were made from 43 samples of tablets made by three manufacturers while 152 samples made by the remaining 27 firms produced only eight complaints with respect to quality.

CLIFTON J. LATIOLAIS

PYROGENS, INACTIVATION BY RADIATION

The Inactivation of Pyrogens with Gamma Radiation, Whittet, T. D. and Hutchinson, W. P., Pharm. J. 179:301 (Oct. 12) 1957.

The authors studied the effects of *gamma* radiation on pyrogens which are a possible source of contamination in plasma. Pyrogens used were London tap water and a purified pyrogen from *Salmonella abortus aqui* (Pyrexal). Cobalt-60 was the source of *gamma* radiation. Rabbits were injected intravenous doses of 10 ml./kilo body weight of tap water and 0.5 ugm./kilo body weight of Pyrexal. A dose of London tap water usually gives a 1.5 deg. C. temperature rise, whereas the Pyrexal dose represented about 250 times the dose which usually gives a 0.6 deg. C. rise.

Results showed that doses of *gamma* radiation up to 7.5 million rep. did not destroy the pyrogens sufficiently to enable samples of tap water to pass the B.P. pyrogen test. Doses of 10 million rep. and over practically completely destroyed the pyrogenicity and samples so treated easily passed the B.P. pyrogen test. A *gamma* radiation dose of 22.5 million rep. was required to destroy the pyrogenicity of the Pyrexal solution. This was a severe test, since the amount of pyrogen in the Pyrexal was about 250 times that necessary to produce sufficient temperature rise in rabbits to fail the B.P. test.

CLIFTON J. LATIOLAIS

CONTROL OF STAPHYLOCOCCAL HOSPITAL SEPSIS

Environmental Disinfection—A Factor in the Control of Staphylococcal Hospital Sepsis, Klarmann, E. G., Am. J. Pharm. 129:42 (Feb.) 1957.

While problems of infection and cross-infection in hospitals have been concerned primarily with hemolytic streptococci in former periods, staphylococcal complications have ascended with the increasing emergence of bacterial strains resistant to antibiotics. Disinfectant measures are involved with the control of bacterial contamination, actual or suspected, personal or environmental.

The inter-related pathways of staphylococci infections are discussed and illustrated indicating the source (the skin, nose, and lesions of the patient and hospital personnel), the transmitting agents (air, instruments, dressings, dust, bedclothes), and finally the infection of the wound.

In one significant report cited, there was found a 95 percent reduction of bacterial contamination from a routine disinfection with an o-phenylphenol disinfectant solution off the floor of a recovery room and connecting entrance hall despite the daily traffic of personnel bringing in fresh contamination, and a simultaneous 60 to 80 percent reduction of bacterial air count. This relationship of surface disinfection and reduction of bacterial air contamination has established that disinfection control on critical surface areas (floor, furniture, etc.) can go far in reducing the risk of air-borne contamination by staphylococci and other pathogens.

In the experimental investigation testing phenol and o-phenylphenol (alone or in combination with other phenolic compounds) against antibiotic-resistant staphylococcal strains, it was found that the bacterial strains did not show increased resistance to phenol and the other phenolic disinfectants. It was also concluded (1) that disinfectants used in hospitals should be irreversibly germicidal, rather than inhibitory, and non-selective in action against several pathogens and antibiotic-resistant strains, and (2) that disinfectants possess a residual action to oppose the reinfection of the treated surface soon after disinfection.

NORMAN HO

PARENTERAL SOLUTIONS CONTAINING PROCAINE AND GLUCOSE

Equilibrium of Procaine-N-Glucoside Formation in Parenteral Solutions Containing Procaine and Glucose, Ikeda, K., Pharm. Bull. (Japan) 5:101 (April) 1957.

Upon storage of procaine injection containing glucose, the formation of procaine-N-glucoside causes a decrease in the anesthetic activity of the procaine.

In this study, the chemical change in this type of preparation was investigated from the standpoint of chemical equilibrium. It was discovered that storage at higher temperatures produced the smallest amount of procaine-N-glucoside.

Calculations in this study show that 1.438% of procaine hydrochloride must be used to prepare 0.5% procaine solution containing glucose at a temperature of 20 degrees while only 0.679% of procaine is needed at a temperature of 100 degrees. Also, 66.5% of the procaine hydrochloride combined with the glucose at 20 degrees while only 26% of the procaine combined at a temperature of 100 degrees.

From these results it was concluded that this type of preparation should be prepared at a high temperature, that heat sterilization will not affect the preparation and that it should not be stored in a refrigerator.

RICHARD E. MARTIN

COMPATIBILITIES OF SURFACTANTS WITH FUNGICIDES

Application of Surface Active Agents to Pharmaceutical Preparations. III. The Influence of Non-ionic Surfactants on the Activity of Sparingly Water-Soluble Fungicides, Aoki, M. et al, J. Pharm. Soc. Japan 77:1071 (Oct.) 1957.

Examinations were made to see whether the decrease of antifungal effect of p-hydroxybenzoic acid esters when solubilized with the non-ionic surface active agents would also occur in other antifungal agents sparingly soluble in water, using phenylmercuric pentachlorophenoxide, Actamer, and G-11, against *Aspergillus niger* and *Trichophyton rubrum*. Addition of non-ionic surfactant was found to decrease the potency of these antifungal agents. It was also recognized, as reported in the previous papers, that the concentration of the antifungal agent in the aqueous phase is more important than that in the micelle of the surface active agents. In aqueous solution, G-11 is more powerful than Actamer in antifungal activity but loses its effect with smaller amount of surfactant because it easily enters into the micelle. By using eight kinds of structurally different non-ionic surfactants it was observed that the following five factors changed the effect of the surfactants on the potency of antifungal agents: balance of hydrophilic and lipophilic parts, additive polymerization degree of ethylene oxide, number of ester bond, difference in fatty acid and the presence of a benzene ring.

AUTHOR'S SUMMARY

QUALITY OF GUAR GUM

A Comparative Study of Commercially Available Guar Gums, Schlakman, Irving A. and Bartilucci, Andrew J., Drug. Stand. 25:149 (Sept.-Oct.) 1957.

In using guar gum, some pharmaceutical formulators have obtained varied results in their products. In this study, the authors carried on an experimental investigation to determine the cause for the disparity in results among formulators.

Thirteen samples of pharmaceutical grade guar gum were obtained from ten suppliers. The following determinations were made on each sample: viscosity and pH of 1% dispersions, carbohydrate or gum, moisture, protein and acid insoluble residue content and fineness of powder analysis. Significant differences in viscosity and particle size were noted in the various samples; whereas, there was a lack of significant difference in gum content.

From these tests, the authors conclude that there appears to be a relationship between the rate of hydration and the particle size of guar gum. The important characteristics upon which the pharmaceutical uses of guar gum are dependent appear to be viscosity of dispersion, particle size and rate of hydration. It is suggested by the authors that the formulator select the guar gum to suit his particular needs based upon satisfactory experimental work and an examination of the specifications provided by the supplier. Once this has been established, the specifications of the satisfactory gum should be written in subsequent purchase orders.

CLIFTON J. LATIOLAIS

STABILITY OF VITAMIN B_{12}

The Stability of Vitamin B_{12}. Protection by Iron Salts Against Destruction by Aneurine and Nicotinamide, Mukherjee, S. L. and Sen, S. P., J. Pharm. Pharmacol. 9:759 (Nov.) 1957.

Vitamin B_{12} has been found to deteriorate progressively when combined in solution with thiamine hydrochloride and nicotinamide. The authors, working with vitamin B-complex and liver extract solutions at a pH range of 4 to 4.5, found deterioration to be complete after three months at room temperature. The cause of the decomposition was not fully explained. The addition of 0.5 mg./ml. of ferric chloride to the solutions prevented any loss of B_{12} activity for a period of four months. Salts of cobalt, manganese, copper, and lead did not protect the vitamin.

JOHN D. LUCASSE

ASSAY FOR CORTISONE AND RELATED STEROIDS

Colorimetric Assay for Cortisone, Hydrocortisone, and Related Steroids, Schulz, E. P. and Neuss, J. D., Analyt. Chem. 29:1662 (Nov.) 1957.

A colorimetric assay based upon the reaction of steroids with 2, 6 - di-tert-butyl-p-cresol (DTBPC) has been developed for the quantitative determination of cortisone, hydrocortisone, and related steroids. Hydrocortisone and other steroids with hydrogen or hydroxyl at position 11 react with DTBPC to give a blue color. Cortisone, representative of those steroids with a ketone at position 11, develops a yellow-brown color. Steroids having a second double bond at positions 1 and 2 (prednisone, prednisolone) produce no color.

The method involves refluxing an alkaline solution of steroid and DTBPC at 100°C with stirring for 30 minutes. Subsequently, absorbance is determined with a spectrophotometer. The analysis may be applied to suspensions, lotions and ointments if the steroid is first dissolved in alcohol. Formulations containing substances which darken upon heating (sodium carboxymethylcellulose, dextrose) require a preliminary extraction with chloroform to separate the steroid from these interferring agents.

JOHN D. LUCASSE

FLOW CHARACTERISTICS OF EMULSIONS

The Rheology of Oil-in-Water Emulsions Part II, the Microscopical Appearance of Emulsions in Laminar Flow, Axon, A., Pharm. J. 179:259 (Sept. 28) 1957.

Using a special microscope cell the author examined the flow characteristics of emulsions of cetyl alcohol, sodium lauryl sulfate and liquid paraffin. In unautoclaved emulsions the globules of dispersed phase were associated in loose clusters with each globule free to move independent of the other. Autoclaved emulsions containing bentonite showed compact "floccules;" the individual globules being surrounded by a hydrated layer of bentonite which restricted their movement. Autoclaved emulsions without bentonite showed no restriction of movement of dispersed globules.

JOHN D. LUCASSE

ELECTRON STERILIZATION OF PHARMACEUTICALS

The Electron Sterilization of Certain Pharmaceutical Preparations, Colovos, G. and Churchill, B., J. Am. Pharm. Assoc., Sci. Ed. 46:580 (Oct.) 1957.

Extensive stability studies were done on penicillin and multivitamin preparations in their final packages which had been exposed to an adequate sterilizing dose of 2×10^6 REP of cathode rays. The accumulated data of these products stored for four years at 25°C indicated (1) that the irradiated material was just as stable as the non-irradiated, and (2) that there was significant increase in acute and chronic toxicity due to irradiation.

However, doses from 8.3 to 20×10^6 REP resulted in the attack on the aromatic ring in procaine and sodium penicillin G and the B lactam function in potassium penicillin G. It was further observed that the acute toxicity of these super irradiated penicillins increased with increasing irradiation dosages.

The use of irradiated products, such as multivitamins, penicillins, cortisone acetate suspensions, and ACTH, clinically has produced no unfavorable reactions. When lyophilized plasma was treated with 2×10^6 REP, a tendency toward breakdown of the plasma proteins was noted

in the electrophoretic analysis. Treated dog plasma showed no untoward reactions, clinically or pathologically, upon reinfusion into dogs.

High antibiotic-yielding mutants of *Penicillin chrysogenum*, *Streptomyces fradiae*, and *Streptomyces erythreus* were isolated from cultures treated with cathode rays.

NORMAN HO

FILTRATION

Experiences with a P.V.C. Filter Medium, Darwin, K. V. and Dee, G. M., Pharm. J. 179:133 (Aug. 24) 1957.

Microporous polyvinyl chloride sheets have been used at the Manchester Royal Infirmary to clarify perfusion fluids for two and a half years. The P.V.C. sheet used is Grade M which is 0.030 inches thick, 20 cm square and is the 2 micron size. Advantages of this filter medium are that it does not lose its strength when wet, it does not shed particles or fibres during filtration, and a rapid rate of filtration can be achieved in a filter press when 4 sheets are used.

After the hospital had been informed by the manufacturer that the sheets were slightly contaminated with lead, tests were carried out to determine whether or not the perfusion fluids contained more than the B.P. limit of lead. Twelve types of perfusion fluids were tested. All fluids contained less than 0.1 p.p.m. of lead prior to filtration and between 0.1 and 0.2 p.p.m. after filtration. Ten litres of distilled water had been pumped through the sheets previous to filtration.

Since the average human blood level for lead is 0.31 p.p.m., it was decided that, provided a limit of not more than 0.2 p.p.m. of lead be maintained, this method of filtration would continue to be used.

FRANZ W. GEISZ

FILTRATION

Filtration with Microporous P.V.C. Sheets, Van Abbe', N. J., Pharm. J. 179:376 (Nov. 9) 1957.

The possibility of using microporous sheets of polyvinyl chloride as a filter-medium in large-scale operations was investigated. A comparison of the rate of flow using two grades of P.V.C. (Porvic Grade M & S) with the standard Sterimat Grade FCB filter pads was conducted.

The Porvic M & S yielded a greater initial throughput than the Sterimat FCB with a lauryl sulfate detergent solution; the flow remained faster throughout the tests. Porvic M & S resisted blockage for a longer period than the Sterimat FCB when a cough linctus containing 50% w/w sucrose was filtered although filtration rates were all unsatisfactory at the pressure used. Pressure was kept constant at 10-12 lbs./sq. in. and a suspension of 0.5% kaolin was added to each solution.

The results obtained with the P.V.C. sheets were considered moderately favorable, but the flow-rates would not seem to be adequate for large-scale filteration of viscous fluids.

FRANZ W. GEISZ

STABILITY OF THIAMINE SALTS

Stability of Drug Preparations II. Stability of Various Thiamine Salts in Preparations. (2) Yamamoto, R., Takahashi, T. and Inazu, K., J. Pharm. Soc. Japan 77:82 (Jan.) 1957.

Stability of various thiamine salts, possessing different solubility in water and different acidity, was examined by preparing into powders compounded with wheat starch, precipitated calcium carbonate, ascorbic acid, or calcium ascorbate. It was thereby found that the stability of thiamine in powder preparations is chiefly dependent on the solubility of thiamine salts, the sparingly soluble salts being stable in principle. In the combination with calcium carbonate, which is a weakly acid salt, the neutral (mono) salts of thiamine were not affected but the acidic (di) salts seem to undergo reaction in the presence of water and the stability decreased in some of the sparingly soluble salts. In combination with ascorbic acid, due to its acidity, mono-salts of thiamine underwent change and their stability decreased, but the acidic salts, especially their sparingly soluble salts, were stable. The use of calcium ascorbate in place of ascorbic acid makes sparingly soluble thiamine monosalts markedly stable.

AUTHOR'S SUMMARY

GLYCEROL, INTRAVENOUS

Fate of Intravenously Administered Glycerol, Zilversmit, D. B. and McCandless, E. L., Proc. Soc. Exp. Biol. Med. 95:755 (Aug.-Sept.) 1957.

Glycerol dissolved in aqueous isotonic solutions of sodium chloride or dextrose and administered intravenously to dogs rapidly disappears from the blood stream. Single injections of 6 Gm. did not produce excessive urinary excretion of glycerol but 12 Gm. led to excretion of one-third the dose. Daily infusions of large doses of glycerol produced marked polyuria and in some animals led to tremors and convulsions. These disturbances were not caused by accumulation of glycerol in the blood. Tremors and convulsions appeared in most dogs receiving more than 5 Gm. glycerol per Kg. body weight, but only after repeated injections. In several animals, it appeared that the occurrence of convulsions sensitized the animal to subsequent infusions.

The authors also used glycerol as a dispersing agent for oil and lecithin to prepare an anhydrous fat emulsion which could be diluted with 5 percent dextrose to furnish high caloric fluid for intravenous use.

DON E. FRANCKE

COMPATIBILITY OF CARBOPOL WITH PRESERVATIVES

The Compatibility of Certain Preservatives with Carbopol 934, Schwarz, T. W. and Levy, Gerhard, Drug. Stand. 25:154 (Sept.-Oct.) 1957.

Carbopol 934*, an anionic carboxylic vinyl polymer useful in pharmaceutical products as a hydrophilic colloid of high thickening capacity, has been evaluated for its compatibility with commonly used preservatives.

Factors tested were viscosity and antibacterial activity of solutions containing 0.5% colloid and various amounts of commonly used preservatives. Preservatives used were: benzalkonium chloride, benzethonium chloride, benzoic acid, sodium benzoate, methyl and propyl parabens, phenol, phenylmercuric acetate, and thimerosal.

Results showed that when used in concentrations generally employed for antibacterial effect, only benzoic acid and sodium benzoate produced a significant decrease in solution viscosity. Also, at these concentrations all solutions were transparent even though the cationic benzalkonium chloride, benzethonium chloride, and phenylmercuric acetate could be expected to react with the anionic colloid. The tests for bacterial growth indicated no impairment of antibacterial activity of the preservatives. Though expected, the cationic preservatives gave no evidence of being inactivated.

JOHN D. LUCASSE

*Available from B. F. Goodrich Chemical Company, Cleveland, Ohio

BETA-PROPIOLACTONE, A STERILIZING AGENT

Beta-Propiolactone for the Sterilization of Biological Materials, LoGrippo, G. A., Henry Ford Hosp. Med. Bull. 5:94 (June) 1957.

Beta-propiolactone (BPL) has been reported as a more satisfactory sterilizing agent against viruses, bacteria, fungi, spore forms of bacteria and fungi, and malignant cells. Sterilization can be achieved at drug concentrations which are not deleterious to tissue proteins. BPL has been employed successfully for (1) the sterilization of human plasma, (2) the sterilization of tissue supplied from autopsy material for use in the operation of a human tissue bank, and (3) the preparation of inactivated virus vaccines.

Beta-propiolactone is a colorless, stable liquid in a concentrated state but is unstable in aqueous solutions. It can be stored satisfactorily in plastic containers or in Neutraglass sealed ampuls at -20 to -30°C. It has a specific gravity of 1.149 and is 37.5 percent (by volume) soluble in water. It reacts readily with hydroxyl, amino carboxyl, sulfhydryl and phenolic groups, all of which are associated with proteins.

Plasma treated with 0.35 percent BPL, and ultraviolet irradiation as recommended by the National Institutes of Health, produces a product which is clear and amber in appearance, stores well under refrigeration, and is well-tolerated by patients. Concentrations used to sterilize human tissue and plasma were not reported. However, results were stated to be very satisfactory and 31 references on beta-propiolactone were given

Beta-propiolactone is available from the B. F. Goodrich Company.

DON E. FRANCKE

LUBRICATING JELLY

A New Lubricating Jelly, Levy, Gerhard and Schwarz, T. W.; Drug and Cosmetic Industry, 81:606 (Nov.) 1957.

A water-soluble lubricating jelly, prepared from synthetics rather than natural gums, is described. This jelly is thermostable and may be sterilized by steam under pressure. The formulation that is presented is transparent, stable and has bacteriostatic properties.

The lubricating jelly proposed contains: Methocel 90 HG 4000 (Dow Chemical Company), Carbopol 934 (B. F. Goodrich Chemical Company), Propylene Glycol, Methylparaben, Propylparaben and distilled water. The formula is adjusted to pH 7 with sodium hydroxide.

The Methocel is a high viscosity hydroxypropylmethylcellulose which is not likely to precipitate from aqueous solutions at elevated temperatures. Oral ingestion toxicity studies have indicated the safety of Methocel 90 HG 4000.

Carbopol 934 is considered as a carboxylic polymer of high molecular weight. These gels are transparent when neutralized with a suitable base and have a high yield strength i.e. they will not flow until the stress applied to them exceeds a minimum value, the yield value. Carbopol 934 has been used in this formula to eliminate excessive tackiness and the dripping tendency of the Methocel 90 HG 4000. After several months of clinical testing, it has been found that Carbopol 934 is neither a primary irritant nor a sensitizer.

The propylene glycol functions as a humectant as well as a lubricant. The bacteriostatic effect of propylene glycol against bacteria and molds is also an important consideration for its incorporation in a lubricating jelly.

The methyl and propylparabens are esters of p-hydroxybenzoic acid which are neutral preservatives effective in low concentration against fungi and Gram-positive bacteria, however, less effective against Gram-negative organisms. The parabens are sufficiently thermostable to permit autoclaving for a period of 30 minutes at a temperature of 120° C. at pH 3 to 8.

The heat stability of these synthetic substances* (*Methocel 90 HG 4000 and Carbopol 934) is illustrated by the fact that they retain their viscous properties even after exposure to heat under pressure. Natural gums do not retain their properties of viscosity in a comparable study. Sodium alginate as well as sodium carboxymethylcellulose show great reduction in their viscosity after exposure to autoclaving.

The formulation presented exhibits good shelf-life properties. There was no apparent loss of viscosity after nine months storage at 42°C.

The jelly possesses the following properties thought to be characteristic of a good lubricating jelly: a) water washable, b) nonirritating, c) easy spreading, d) non-dripping, e) good adherance to instruments, f) bacteriostatic, and g) permits sterilization by autoclaving.

EDWARD A. SUPERSTINE

THEOPHYLLINE SALTS, SOLUTION RATES

Solution Rate of Theophylline Salts and Effects from Oral Administration, Nelson, E., J.Am.Pharm.Assoc., Sci.Ed. 46:607 (Oct.) 1957.

Several salts of theophylline were dissolved in various mediums possessing hydrogen ion concentrations in the physiological range to determine the fundamental reasons for the clinical differences of blood levels from the oral administration of theophylline salts. Among the theophylline compounds used were theophylline and the theophyllinate of choline, ethanolamine, ethylenediamine, isobutanolamine, and isopropanolamine. The dissolution rates were determined at 25° C. in 0.1N HCl, in 0.1M phosphate buffer solution with pH 6.7, and in 0.1M borate buffer solution with pH 8.87. The experimental method was described in detail.

The results of the experiment were correlated with theoretical mathematics, which described the rate of solution process or the Noyes-Whitney Law. According to the theory, a diffusion layer, that is, a fine film of liquid saturated with a dissolving solid, is present at the liquid-solid interface and the rate of solution is controlled by the diffusion of material through it, other factors being constant. Furthermore, the rate of solution would depend upon the pH of the diffusion layer. If the dissolution medium was acidic, the rate of solution of salts would be rapid as compared to the rate at which the acid would dissolve.

It was found that differences in solution rate existed between theophylline and its salts and that the rates were relatively independent of the buffer pH. Depending upon the dissolution medium, the choline and isopropanolamine salts dissolved faster than the ethylenediamine salts with theophylline dissolving the slowest. When theophylline was studied in acidic and basic media, the expected increase in solution rate was observed.

The results indicated the existence of the diffusion layer. The approximate correlation between solution rate and the pH of the diffusion layer was determined and mathematically expressed. The correlation between the water solubility and the solution rates of the theophylline compounds was poor, although water solubility has a part in determining solution rate.

Since the experimental results strongly pointed out that the solution rate is the fundamental factor in explaining the clinical results of different blood levels previously reported, a mathematical scheme was derived in which the solution rate, with other factors being constant, determines the rate of buildup of blood level and maximum blood level. The following scheme was depicted: A⟶B⟶C⟶D, where A represents the solid drug at the absorption site, B the drug in solution at the absorption site, C the drug in the blood, and D the degraded drug. The conclusions arrived at in this experiment would also apply for salts of poorly soluble, weak acids with weak and strong water-soluble bases.

NORMAN HO

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION
—General

Vanderwarker, Richard D.: The Art of Decision Making, *Hospitals* 31:36 (Dec. 1) 1957.

—Costs

Wing, W. T.: Hospital Departmental Costing: The Pricing of Medical and Surgical Supplies, *Public Pharmacist* (Great Britain) 14:222 (Oct.) 1957.

—Purchasing

Terenzio, J. V.: Some Legal Aspects of Hospital Purchasing, Part III, *Hosp. Management* 84:101 (Dec.) 1957.

DETAILING

Zugich, John J.: Code for Detailing in Hospitals, *Am. Profess. Pharm.* 23:980 (Nov.) 1957.

HISTORY

Sister M. Frances: The History of the Canadian Society of Hospital Pharmacists, *Hosp. Pharm.* (Canada) 10:269 (Sept.-Oct.) 1957.

NARCOTICS

Oddis, Joseph A.: Control of Narcotics (Straight from Headquarters) *Hospitals* 31:40 (Nov. 16) 1957.

PARENTERAL SOLUTIONS

(Includes Central Sterile Supply)

Anderson, Mary Helen: Central Service: The Pharmacist As a Central Service Supervisor, *Hosp. Management* 84:76 (Dec.) 1957.

Carter, D. V.: Filtered Air Supplies For Sterile Rooms, *Public Pharmacist* (Great Britain) 14:230 (Oct.) 1957.

PHARMACY AND THERAPEUTICS COMMITTEE
—Investigational Drugs

Actions by American Hospital Association's Board of Trustees: Investigational Drugs in Hospitals, *Hospitals* 31:106 (Dec. 1) 1957.

SMALL HOSPITALS

Berman, Alex: Pharmacy Service in Small Hospitals, *Am. Profess. Pharmacist* 23:1066 (Dec.) 1957.

Berman, Alex and Poole, M. Alan: There's No Substitute for the Pharmacist, *Modern Hosp.* 89:94 (Dec.) 1957.

Moravec, Daniel F.: Pharmacy Service In Smaller Hospitals, Part II, *Hosp. Management* 84:108 (Dec.) 1957.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

The following monographs and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *Journal* to November 30, 1957.

NOTICE

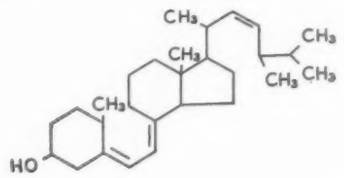
New and Nonofficial Remedies 1957 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1957 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to October 1956. The index listed below contains those drugs evaluated and published between October 1, 1956 and November 30, 1957.

INDEX TO EVALUATED DRUGS, THIS ISSUE

INDEX TO EVALUATED DRUGS PUBLISHED IN THE JANUARY-FEBRUARY, MARCH-APRIL, MAY-JUNE, JULY-AUGUST, SEPTEMBER-OCTOBER, AND NOVEMBER-DECEMBER 1957, ISSUES OF THE BULLETIN, NOW THE AMERICAN JOURNAL OF HOSPITAL PHARMACY.

Dihydrotachysterol — Hytakerol®

Dihydrotachysterol is 9, 10,-secoergosta-5, 7, 22-triene-3β-ol.—Dihydrotachysterol is prepared in noncrystalline form as an oil solution, which is standardized biologically and adjusted to a potency equivalent to 1.25 mg. of the crystalline material per cubic centimeter. The structural formula of dihydrotachysterol may be represented as follows:



Actions and Uses

Dihydrotachysterol is obtained by the reduction of tachysterol, a derivative of irradiated ergosterol. Chemically, however, it is more closely related to calciferol (vitamin D_2), differing from it structurally in that the $=CH_2$ group at C-19 is reduced to $-CH_3$, with the elimination of the double bond. This difference is responsible for the fact that dihydrotachysterol has only a small fraction of the antirachitic potency of calciferol (1/400 to 1/500), although it retains the ability to raise the calcium concentration of the blood. Because of its chemical similarity to calciferol and its strong "calcemic" activity, for which it is chiefly used in therapy, the current trend is to regard it as a form of vitamin D.

Dihydrotachysterol, when administered in appropriate doses, raises the level of total calcium and, consequently, the concentration of ionic calcium in the serum. Because of this calcemic effect, it is of value in correcting the hypocalcemia of hypoparathyroidism (idiopathic or postoperative) and pseudohypoparathyroidism, thereby controlling tetany and preventing cataract formation and other manifestations of hypocalcemia. Another important use of dihydrotachysterol, presumably also dependent upon its calcemic effect, is in the treatment of vitamin D-resistant rickets. Its effectiveness in this disease appears to equal the effectiveness of large doses of calciferol. Dihydrotachysterol may be given orally over considerable periods of time, provided that the serum calcium is not permitted to rise above normal levels.

The weight of evidence at the present time is that four substances, namely, calciferol (vitamin D_2) vitamin$_3$, dihydrotachysterol, and parathyroid hormone, all have a direct effect on the mobilization of mineral from bone, and that this effect is partially responsible for the elevation of serum calcium when using each of the preparations. It seems unlikely that minor differences in the physiological effects of these preparations, such as in their effects upon serum and urine phosphate, would prove decisive in the choice of an activated sterol for the control of hypocalcemia. The same may be said concerning even the major differences in their influence upon the absorption of calcium from the intestines. Except for the fact that dihydrotachysterol appears to act more rapidly and to be more rapidly disposed of when its administration is discontinued, there seems to be little ground for a choice between calciferol and dihydrotachysterol, either on the basis of the effectiveness of the calcemic action, common to both, or of relative toxicity or other undesirable side-effects. Both of these preparations are useful, and the selection of one for use is largely a matter of individual preference. Possibly the recent suggestion that the medication be changed occasionally from one preparation to the other in the course of long-continued replacement therapy will prove of value.

Dihydrotachysterol has been reported to have beneficial effects in treating scleroderma, but this evidence is scanty and inconclusive. Successful use in the tetany of pregnancy has also been reported, but the desirability of such use has

been questioned. Administration of dihydrotachysterol or any other preparation to raise the serum calcium level is contraindicated in hypocalcemia associated with renal insufficiency and hyperphosphatemia.

Dihydrotachysterol, like calciferol, is a highly potent preparation. The doses required to maintain the serum calcium at or near the normal level border on those doses that are definitely toxic. For this reason either preparation must be used with extreme care, especially during the initiation of therapy when the dosage for the individual is being established. After this has been accomplished, the Sulkowitch test for excessive excretion of calcium in the urine is a useful adjunct to therapy.

Dosage

Dihydrotachysterol is administered orally either as an oil solution of which 1 cc. is equivalent to 1.25 mg. of the crystalline material, or in capsules each containing 0.5 cc. of the solution or the equivalent of 0.625 mg. of crystalline dihydrotachysterol. For the treatment of the hypocalcemia of hypoparathyroidism or of vitamin D-resistant rickets, therapy is initiated with relatively high doses. These range from 3 to 10 cc. (or 6 to 20 capsules) per day for several days. Maintenance doses average 1 to 7 cc. (or 2 to 14 capsules) per week, depending upon the blood and urine calcium levels.

Preparations: capsules 0.625 mg.; solution 1.25 mg. in 1 cc.
Applicable commercial name: Hytakerol.
J.A.M.A. 165:1141 (Nov. 2) 1957.

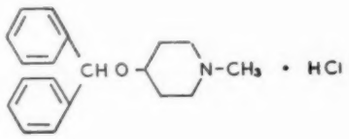
Preparations

Capsules Dihydrotachysterol (Hytakerol) 0.625 mg.
Solution Dihydrotachysterol (Hytakerol) 1.25 mg. per ml.; 15 ml. bottles.

Diphenylpyraline Hydrochloride

Diafen® Hydrochloride

DIPHENYLPYRALINE HYDROCHLORIDE is 4-diphenylmethoxy-1-methylpiperidine hydrochloride.—The structural formula of diphenylpyraline hydrochloride may be represented as follows:



Actions and Uses

Diphenylpyraline hydrochloride, a potent antihistaminic compound, is related chemically and pharmacologically to diphenhydramine. Although clinical experience with the drug is limited, it appears to be satisfactory for the treatment of allergic and hypersensitivity reactions usually considered amenable to therapy with histamine-antagonizing agents. The incidence of side-effects to diphenylpyraline hydrochloride is low; drowsiness, dryness of the mouth, headache, and dizziness are encountered occasionally. See the general statement on histamine-antagonizing agents in New and Nonofficial Remedies.

Dosage

Diphenylpyraline hydrochloride is administered orally. The usual dose for adults is 2 mg. every four hours. Dosage for children is reduced according to age.

Preparations: tablets 2 mg.
Applicable commercial name: Diafen.
Schenley Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of diphenylpyraline hydrochloride.
J.A.M.A. 165:1142 (Nov. 2) 1957.

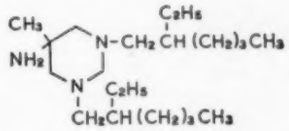
Preparations

Tablets Diphenylpyraline (Diafen) Hydrochloride 2 mg.

Hexetidine

Sterisil®

HEXETIDINE is 5-amino-1, 3-bis(β-ethlylhexyl)-5-methylhexahydropyrimidine.—The structural formula for hexetidine may be represented as follows.



Actions and Uses

Hexetidine, a local anti-infective agent, is proposed for use in the treatment of vaginitis and cervicitis due to the fungal organism, Candida albicans, or the protozoan organism, Trichomonas vaginalis. The drug is also reported to be effective against a newly named organism, Hemophilus vaginalis, which is said to be the etiological agent responsible for most cases of so-called nonspecific bacterial vaginitis and leukorrhea. In laboratory susceptibility tests, hexetidine shows moderate to excellent antimicrobial activity against these organisms as well as against some gram-positive and gram-negative bacteria. However, the in vivo (clinical) evidence is not nearly so convincing. Although prior experience has shown that the protozoan Trichomonas vaginalis is readily destroyed by a variety of agents in the laboratory, there is frequently very little correlation between in vitro and in vivo activity. Thus, while the protozoan is susceptible to hexetidine in the test tube, this does not necessarily indicate an equal antimicrobial activity in clinical infections.

The drug has been used in a fairly large number of patients with trichomonal vaginitis, and, in some cases, considerable improvement has been noted. However, in view of the difficulty in enforcing strict controlled conditions and obtaining adequate follow-up observations in studies of this nature, it is not yet possible to determine the usefulness of hexetidine in comparison with other agents. Hence, additional controlled clinical studies are needed before the ultimate usefulness of hexetidine as a trichomonacide can be determined. Results of clinical trials with hexetidine in vaginal moniliasis have been somewhat more encouraging than in trichomonal infections. Some observers have reported high rates of cure after a course of therapy with this agent. Since the monilial infections are, in general, more amenable to therapy of any kind than are trichomonal infections, the significance of the reported high rates of cure in vaginal candidiasis is uncertain. On the basis of present evidence, hexetidine appears to be of about the same order of effectiveness as gentian violet but has the advantage of not staining clothing. Case reports suggest that hexetidine is clinically effective in some cases of nonspecific vaginitis believed due to H. vaginalis.

The systemic toxicity of hexetidine in experimental animals is low. Except for occasional instances of local irritation, clinical employment of the drug has not been associated with any untoward reactions or side-effects. Its sensitizing potential on the mucosa of the vagina has not been determined.

Dosage

Hexetidine is employed intravaginally as a 0.1% gel. The suggested dosage is approximately 7 cc. of the gel instilled high in the vaginal vault on each of six nights. The treatment may be repeated if necessary, and the drug may be used throughout the menstrual period. A douche may be used prior to application. Soapy solutions should not be used for douching since the drug is inactivated by soap. Hexetidine should not be used intracervically.

Preparations: gel (vaginal) 0.1%.
Applicable commercial name: Sterisil.
Warner-Chilcott Laboratories, Division of Warner-Lambert

Pharmaceutical Company, cooperated by furnishing scientific data to aid in the evaluation of hexetidine.

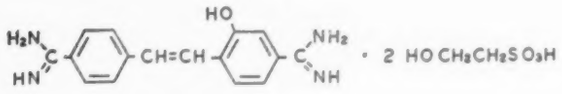
J.A.M.A. *165*:1142 (Nov. 2) 1957.

Preparations

Gel, Vaginal, Hexetidine (Sterisil) 1.5 oz. tubes, with 6 disposable applicators.

Hydroxystilbamidine Isethionate

HYDROXYSTILBAMIDINE ISETHIONATE is 2-hydroxy-4, 4′-stilbenedicarboxamidine di(β-hydroxyethanesulfonate).—The structural formula of hydroxystilbamidine isethionate may be represented as follows:



Actions and Uses

Hydroxystilbamidine isethionate, an aromatic diamidine base, is a derivative of stilbamidine isethionate and exerts the same type of antifungal-antiprotozoan activity as the latter agent. The chemotherapeutic spectrum of hydroxystilbamidine appears to be identical with that of its predecessor, stilbamidine. The chief difference between these agents lies in the fact that whereas stilbamidine frequently produces a late trigeminal neuropathy, this has not been observed with use of hydroxystilbamidine. This difference is considered sufficiently important to warrant replacement of stilbamidine by the equally effective, but less toxic, hydroxy-derivative.

Hydroxystilbamidine isethionate appears to be the best chemotherapeutic agent available for the treatment of North American blastomycosis. Adequate therapy will frequently lead to complete eradication of severe pulmonary and systemic infections which, prior to the introduction of the diamidine compounds, were considered incurable. Hydroxystilbamidine may also be used in conjunction with iodine and roentgen therapy for the treatment of the localized or cutaneous forms of the disease. Although no data are as yet available, it is possible that the drug may also be of some usefulness in South American blastomycosis and coccidioidomycosis. It is of no value in the treatment of Torula infections or histoplasmosis.

Hydroxystilbamidine is effective for the management of certain types of leishmaniasis. Although antimony compounds are generally considered to be drugs of choice for this protozoan infection, hydroxystilbamidine may frequently produce beneficial effects in patients who fail to respond or are intolerant to antimony-containing agents. The drug apparently is equally useful for American mucocutaneous leishmaniasis and for kala-azar (visceral leishmaniasis).

There is some evidence that actinomycosis is influenced favorably by use of hydroxystilbamidine. However, since this mycotic disease is treated effectively with antibiotics in approximately 80% or more of the cases, hydroxystilbamidine should never be considered a primary therapeutic agent. A trial of therapy with hydroxystilbamidine is warranted in actinomycosis only in those patients who have failed to respond to adequate treatment with the preferred antibiotics.

To date, there are no reports on the use of hydroxystilbamidine in African trypanosomiasis. However, on the basis of its close similarity to stilbamidine, it may be predicted that the hydroxy derivative, like the parent drug, will be effective in early cases of Gambian and Rhodesian trypanosomiasis (African sleeping sickness). Since neither form of the drug gains access to the cerebrospinal fluid nor can be given intrathecally, it cannot be expected to be useful and should not be administered in the late neurological stage of the disease. The diamidines are of no value in South American trypanosomiasis (Chagas' disease).

Because of the common factor of hyperglobulinemia in kala-azar and multiple myeloma, the diamidines have been tried for the treatment of the latter disease. In some patients, such therapy affords marked, but temporary, relief from pain. There is also some evidence that it can cause favorable morphologic changes in the myeloma cells of some patients. However, the response is usually inconsistent, and, even in the most favorable cases, relapse inevitably occurs. There is no evidence that hydroxystilbamidine affects the course of the disease, prolongs the life of patients with multiple myeloma, or causes arrest of the neoplastic process. In general, the use of urethan or roentgen irradiation to localized lesions is considered preferable for the initial treatment of the disease. However, in view of the inadequacies of these and all other modes of therapy, a trial of hydroxystilbamidine may also be justified for the palliation of pain in multiple myeloma.

Aside from the absence of late trigeminal neuropathy, other toxic manifestations referable to hydroxystilbamidine appear to be somewhat less frequent than with use of stilbamidine. However, any of the immediate side-reactions which have been observed during or immediately after intravenous injection of stilbamidine may be expected to occur with the use of hydroxystilbamidine. These effects, believed to be due to the release of bound histamine, include the following: fall in blood pressure, rapid pulse, facial flushing, dizziness, salivation, sweating, headache, nausea, vomiting, dyspnea, formication, syncope, fecal and urinary incontinence, and edema of the eyelids and face. Such side-effects, if present, are usually transitory and disappear within 10 to 30 minutes. They may be minimized by slow intravenous infusion of diluted solutions.

Hydroxystilbamidine isethionate in solution is unstable when exposed directly to heat, sunlight, and ultraviolet light. Such exposure causes partial deterioration of the drug at the unsaturated stilbene linkage with release of toxic breakdown products. Deterioration may be prevented by storing the drug in a dry form away from heat and light. Freshly prepared solutions should be protected similarly. After injection, patients should avoid excessive exposure to sunlight on the premise that toxic products may be formed from the drug remaining in the skin. There is no evidence that freshly prepared solutions of hydroxystilbamidine isethionate are toxic to the kidney or liver. Nevertheless, renal and hepatic function should be evaluated prior to initiating therapy, and the drug should be administered cautiously and in reduced dosage in the presence of renal or hepatic disease.

Dosage

Hydroxystilbamidine isethionate is administered by continuous, slow, intravenous drip and, rarely, by intramuscular injection. For intravenous use, a freshly prepared solution of the dose to be used is diluted in about 200 cc. of either 5% dextrose in water or isotonic sodium chloride solution. This is infused over a period of 45 minutes to 2 hours. Slow infusion is essential to avoid a fall in blood pressure or other side-effects. During infusion, the solution should be protected from light by covering the container with black paper or a heavy towel. At warm temperatures, it may be advisable to complete the injection in somewhat less than 2 hours to avoid dangerous deterioration of the solution.

In occasional cases in which intravenous use is not feasible, it may be necessary to administer hydroxystilbamidine isethionate by the intramuscular route. For such use, the proper amount of the dry, sterile powder is dissolved in 10 cc. of 5% dextrose in water or isotonic sodium chloride solution and is administered by deep intragluteal injection. Since pain at the site of injection follows its intramuscular use, the drug should be given intravenously whenever possible.

For treatment of susceptible fungal or protozoan infections,

the suggested dosage for adults is 225 mg. at intervals of 24 hours. The duration of such therapy is determined by clinical improvement and disappearance of causative agents from the lesions. For example, a course of therapy consisting of daily injections of 225 mg. may be as short as 1 week to 10 days in cases of highly susceptible kala-azar to as long as 2 to 3 months in severe blastomycotic infections. Clinical improvement is the sole criterion for total dosage when the drug is tried as a palliative agent in multiple myeloma. For all indications, dosage for children is reduced proportionally according to body weight or body surface.

Preparations: powder (injection) 225 mg.
Applicable commercial name. Hydroxystilbamidine Isethionate.
The Wm. S. Merrell Company cooperated by furnishing scientific data to aid in the evaluation of hydroxystilbamidine isethionate.

J.A.M.A. 165:1143 (Nov. 2) 1957.

Preparations

Injection Hydroxystilbamidine Isethionate 225 mg. ampuls.

Novobiocin Sodium — Parenteral Use of

The Council has evaluated the parenteral use of the antibiotic, novobiocin (Albamycin, Cathomycin) sodium, for injection by either the intravenous or intramuscular route. On the basis of currently available evidence, the Council concluded that the parenteral administration of this agent is justified as a temporary measure for the treatment of severe infections in those patients who are unable to take the drug by mouth. The indications for parenteral therapy with novobiocin sodium are the same as those for the oral form of the drug. (See the monograph on novobiocin sodium in THE JOURNAL, Feb. 23, 1957, page 646.)

By either parenteral route, the usual dosage for adults is 500 mg. every 12 hours; for children, 15 mg. per kilogram of body weight every day in two divided doses at intervals of 12 hours. For intravenous administration, a concentrated solution is freshly prepared by dissolving 500 mg. of the powdered drug in 5 cc. of a suitable solubilizing agent. This solution is diluted with 30 cc. of isotonic sodium chloride solution, lactated potassic saline injection (Darrow's solution), or Ringer's injection and then administered by slow, direct, intravenous injection. At least 5 to 10 minutes should be allowed for direct intravenous injection, since too rapid administration may cause venous irritation or even thrombophlebitis. If parenteral fluid therapy is also indicated, the concentrated solution of novobiocin sodium may also be added to 1 to 3 liters of any of the foregoing fluids and administered by intravenous infusion. In occasional cases in which neither oral nor intravenous therapy is possible, the concentrated solution (100 mg. per cubic centimeter) of novobiocin sodium may be injected intramuscularly. This, however, usually causes some pain and irritation at the site of injection. Hence, whenever parenteral administration is necessary, the intravenous route is preferred. Oral medication should be substituted for parenteral therapy as soon as possible.

The Council voted to expand the N.N.D. monograph on novobiocin sodium to describe its use by the parenteral route.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of the parenteral use of novobiocin sodium.

J.A.M.A. 165:1145 (Nov. 2) 1957.

Blood Dyscrasias Associated With Promazine Hydrochloride Therapy

Report to the Council

The Council has authorized publication of the following report.
H. D. KAUTZ, M.D., *Secretary.*

The Registry, established under the direction of the Subcommittee on Blood Dyscrasias of the Committee on Research, has received 257 case reports from 74 cooperating physicians in which a dyscrasia was suspected as having been caused by drugs or chemical substances. A review of these reports reveals that 10 cases were apparently associated with the use of the new drug promazine hydrochloride. Since the Registry is intended as a system for the alerting of physicians, it was concluded that the possible association of these cases with the use of this drug was sufficiently suggestive to warrant bringing this fact to the attention of the medical profession.
NORMAN DE NOSAQUO, M.D., *Secretary, Committee on Research.*

A review of the reports received by the Registry since July, 1956, revealed 10 cases of blood dyscrasias apparently associated with promazine (Sparine) hydrochloride therapy. A search of the English-language medical literature to the date of the preparation of this statement has uncovered two case reports of granulocytopenia associated with promazine hydrochloride therapy, one of which is among those reported to the Registry. Wyeth Laboratories has been most cooperative and has supplied an additional record of 8 cases not previously reported to the Registry, bringing the total to 18 cases in which promazine therapy was suspected as being associated with a case of blood dyscrasia. It should be pointed out that in seven instances the patients received other drugs such as chlorpromazine (Thorazine) hydrochloride. Although all of the cases of blood dyscrasias associated with the use of promazine hydrochloride probably have not been reported, it has been suggested that the rate of incidence of a dyscrasia is relatively low.

Although depression of granulocytes was prominent in every case reported, the bone marrow studies in some cases indicated a depression of other cellular elements as well. Of the 18 known cases, we have information that 4 ended fatally. In cases that were identified early, cessation of use of the drug and institution of appropriate measures were usually followed by fairly prompt recovery. Physicians who prescribe promazine hydrochloride should instruct attendants, nurses, and patients to discontinue use of the drug and to report immediately if there is any sudden occurrence of symptoms such as sore throat, or malaise. These instructions must be stressed. The interim blood cell counts alone cannot be relied upon because the condition could develop suddenly between routine examinations.

Wyeth Laboratories has included a forceful warning and has placed it prominently in the leaflet available to the medical profession. The firm should be commended for its diligence and willingness to cooperate with the subcommittee in its effort to bring this matter to the attention of physicians. Since the drug may possess potential for some harm, the subcommittee suggests that physicians limit its use to those conditions in which such use is warranted and avoid its use in the treatment of trivial or minor complaints.

J.A.M.A. 165:685 (Oct. 12) 1957.

Drug Reactions, Enzymes, and Biochemical Genetics

ARNO G. MOTULSKY, M.D., SEATTLE

Report to the Council

Because of the renewed awareness of genetics in relation to the cause of disease and because of an increasing interest in this subject, the following article is most timely. The author has prepared this report at the invitation of the Subcommittee on Blood Dyscrasias of the Committe on Research.
NORMAN DE NOSAQUO, M.D., *Secretary Committee on Research*

In discussions of drug idiosyncrasy, careful distinction should be made between toxic reactions caused by immunologic mechanisms (drug allergy) and abnormal reaction caused by exaggeration or diminution of the usual

From the Department of Medicine, University of Washington Medical School. Dr. Motulsky is a John and Mary R. Markle Scholar in Medical Science.

effect of a given dose.[1] Although some progress has been made in the study of mechanisms of drug allergy, little was known until recently about the pathogenesis of hypersusceptibility reactions and hyposusceptibility reactions. Data are available now which suggest that reactions of this type may be caused by otherwise innocuous genetic traits or enzyme deficiencies.

Hockwald and his co-workers[2] demonstrated that approximately 10% of American Negroes and a very small number of caucasians developed hemolytic anemia when given an average dose of primaquine or chemically related drugs. Beutler and associates[3] showed that red blood cells of susceptible individuals possessed decreased numbers of nonprotein, sulfhydryl groups. It has now been pointed out that primaquine sensitivity is related to glucose-6-phosphate dehydrogenase activity.[4] Investigations of the genetics of this trait, now in progress, suggest that the abnormality is caused by a sex-linked gene of intermediate dominance.[5] The red blood cell abnormality per se has no known deleterious effect on the individual or on red blood cell life span. Excessive doses of primaquine or related drugs appear to produce hemolytic anemia in all individuals. The red blood cells of susceptible subjects lack sufficient enzymatic protection against damage by the drug even with the smaller dosage levels. These investigations explain the greater incidence of hemolytic anemia among Negroes when they were given pamaquine or sulfanilamide in past years. Hemolytic anemia due to naphthalene[5] and nitrofurantion (Furadantin)[6] also has been demonstrated to be associated with the sulfhydryl defect responsible for primaquine sensitivity. Two different in vitro tests to detect susceptibility have been described.[7]

Lehmann and Ryan[8] pointed out that prolonged apnea caused by the muscle relaxant succinylcholine (Anectine, Quelicin, Sucostrin) chloride sometimes can be explained by low levels of pseudocholinesterase. A certain amount of this enzyme is required for inactivation of the drug. The enzyme was found to be diminished in sensitive patients as well as in some of their family members. These findings have been confirmed.[9] The exact mode of inheritance of this familial enzymatic deficiency is still indeterminate. Other causes of pseudocholinesterase deficiency such as malnutrition and liver diseases were ruled out.

It is not unlikely that some drug sensitivity reactions previously characterized as caused by hypersusceptibility may be produced by similar mechanisms. It is also possible that the potential for antibody formation due to haptenes, and therefore susceptibility to drug allergy, is conditioned by genetic factors. Knowledge of the metabolic fate of various drugs and improved methods of studying enzyme and antibody reactions in man promise to provide tools for further approaches to this problem.

Patients with hereditary hyperbilirubinemia (constitutional nonhemolytic jaundice) are likely to be a challenging group for study, since they have been postulated to have deficient enzymatic machinery for the coupling of bilirubin to glucuronides.[10] Since many drugs such as salicylates and sex hormones are excreted as glucuronides, valuable hints may be forthcoming from study of the fate of such drugs in these patients. The precipitation of symptoms of acute intermittent porphyria by barbiturates and alcohol is well known. Further evidence of interference by these agents with the disordered enzymatic reactions responsible for the disease is likely to be found. Megaloblastic anemia is sometimes produced by anticonvulsants.[11] A genetically determined abnormality of folic acid metabolism may be the reason for this complication. Liver damage caused by cinchophen, jaundice induced by chlorpromazine, and cinchonism produced by small doses of quinine or quinidine are other reactions possibly caused by genetic enzymatic defects.

Tolerance to drugs or failure of expected effect with an average dose may have a similar basis. No proved examples due to genetic defects exist in man. Some strains of rabbits, however, can be given large quantities of atropine and related compounds without effect.[12] These animals inactivate atropine by a genetically controlled enzyme, atropinesterase, in the blood and tissues. Marked variability in length of narcosis induced by hexobarbital (Evipal) sodium has been described in various species and in different strains within a species. These differences could be related to variable enzymatic detoxification activity in liver microsomes.[13] Insulin-resistant mouse strains exist which survive 300 times the dose of insulin which kills normal mice.[14]

Qualitative differences between species also exist. A drug effect exhibited by most individuals of one species may be rare in other species. Thus, hyperexcitability due to morphine is the usual response in cats and race horses but occurs rarely in man in whom it is considered an idiosyncrasy. Comparative biochemical studies on drug metabolism may provide clues to such idiosyncrasies.

Another pertinent area for research includes drug reactions involving red blood cell constituents in the newborn. Toxic methemoglobinemia is produced in this age period by exposure to aniline dye-stamped diapers[15] or by ingestion of well-water high in nitrate content.[16] Over 90% of the well-water cases have occurred in children under two months of age.[17] Since the concentration of the red blood cell enzyme required for reduction of methemoglobin to hemoglobin is decreased in the red blood cells of the newborn,[18] it is probable that such enzyme deficiency provides a partial explanation for the maintenance of the abnormal pigment. Red blood cell destruction by excessive doses of menadiol sodium diphosphate (Synkayvite Sodium Diphosphate, Vitamin K Analogue) caused hemolytic anemia and kernicterus in some infants and has been related to low vitamin E levels in cells of infants.[19] The lowered concentration of red blood cell catalase in cells of infants[20] may be one significant factor in susceptibility to vitamin K hemolysis. The previously mentioned sulfhydryl defect associated with a variety of drug sensitivities also may predispose the infant to vitamin K hemolysis.[5]

The detection of hereditary biochemical traits that cause drug reactions may contribute to the progress of human genetics in general. Such traits may be related to susceptibility or resistance to diseases other than drug idiosyncrasies. Some geneticists argue that relatively rare traits such as some of those under discussion could not be maintained in the population at their observed frequency unless such traits provided the carriers with some selective advantage.[21] The general validity of this argument appears to have been confirmed by the demonstration of decreased malaria mortality in infants with sickle-trait and the possible relationship of the ABO blood groups to the frequency of diseases such as ulcer and gastric cancer.

Since a given gene may be more frequent in certain ethnic groups, any drug reaction that is more frequently observed in a given racial group, when other environmental variables are equal, will usually have a genetic basis. Investigations on drug reactions therefore should include careful notation of the ethnic or racial extraction of the patient. Consanguinity, such as in first-cousin marriages among the parents, points to a recessive genetic mechanism and should be inquired about and mentioned. Unfortunately, drug reactions among parents and siblings will not often be elicited when the physician is taking a family history, because families are small and most drugs are new and have not been used for long. Once a possible hereditary defect is identified, family and population surveys are desirable.

Genetically conditioned drug reactions not only are of practical significance but may be considered pertinent models for demonstrating the interaction of heredity and environment in the pathogenesis of disease. In these instances it can be shown clearly how hereditary, gene-controlled enzymatic factors determine why, with identical exposure, certain individuals become "sick," whereas others are not affected. It is becoming increasingly probable that many of our common diseases depend on genetic-susceptibility determinants

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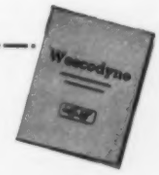

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of this type. Haldane's prediction[22] that "the future of biochemical genetics applied to medicine is largely in the study of diatheses and idiosyncrasies, differences of innate make-up which do not necessarily lead to disease but may do so" has been confirmed by these recent developments in therapeutics.

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Thallotoxicosis A Recurring Problem

Report to the Council

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary.*

Thallium is an extremely toxic chemical. It is one of the more insidious poisons because of the delayed and undistinguishing character of most of its symptoms and because of the difficulty in treating intoxication or preventing disabling after-effects. It is an unfortunate fact that effective baits containing poisons for rat, mouse, and cockroach control usually are food products which are also quite acceptable to children and pets. When this factor is aggravated by careless storage of attractive packages within reach of children, by the fact that there is no legal way to require supervision over the ultimate user, and by the fact that he may overlook proper labeling, it is not surprising that concern over the health hazards of thallium should develop.

This concern is not unfounded, as evidenced by the alarming incidence of thallium poisoning in Texas during the past two years. The growing number of cases of accidental poisoning in children, with pesticidal uses of thallium, threaten to place it in the same disrepute that it presently suffers as a drug and cosmetic. The availability of effective and less toxic insecticides and rodenticides suggests that sanitation and the public welfare would not be penalized by discouraging its use as a household chemical.

BERNARD E. CONLEY, PH.D., *Secretary Committee on Pesticides.*

With the abandonment of thallium as an internal medicament and depilatory, the incidence of accidental injury caused by it in this country has been markedly reduced. Today, the principal uses of thallium are in the control of rats, mice, ground squirrels, prairie dogs, moles, and insects such as ants and roaches. Periodically recurring episodes of poisoning associated with these pesticidal uses focus attention on the dangerous nature of this economic poison, especially when it is used in and around the home.

Thallium sulfate, containing approximately 80% of the metal, is the only form of the poison used in pesticidal formulations. It is a heavy, white, water-soluble salt resembling table salt in general appearance and has a definite astringent taste. This taste apparently is not objectionable to rodents or insects in the concentrations present in baits. It acts as a general cell poison with cumulative properties and a variety of toxic manifestations. Thallium is more toxic than is lead and as pernicious in its effects. Although toxic to plants and to soil, the amounts of thallium contained on poisoned grain used as bait are said to be noninjurious to soil and vegetation.

Thallium is readily absorbed through the skin and from the alimentary tract. It is distributed to all tissues, especially the muscles, spleen, and kidneys. Cumulation may be followed by a sudden release of poison from tissues, such as that which occurs with lead poisoning. It accumulates to some extent in the skin and hair, but, unlike lead, it is not selectively retained in the bones. Thallium is found in all body fluids but is excreted mainly in the urine. In fatal cases, milk may be toxic to sucklings, and thallium poisoning occurring before labor has been reported to be lethal to the newborn infant.

The action of thallium is due to the thallium ion, the univalent form of the metal. It is extremely toxic to all forms of life, and the LD_{50} for humans is in the range of 0.2 to 1.0 Gm. Symptoms of acute poisoning are variable but generally conform to those of heavy metal poisoning. They are referable to the gastrointestinal tract and nervous system. Symptoms develop quite slowly, being delayed from several hours to two days. Digestive disturbances include a metallic taste, salivation, stomatitis, nausea, vomiting, and abdominal pain. Vasomotor disturbances may be reflected in puffiness of the cheeks, eyelids, and lips. Tingling and pain in the hands and feet, muscular weakness, delirium, convulsions, and coma may ensue. Death can occur in a few days or be delayed several weeks. Disintoxication is slow, and recovery requires

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six or more months. Sequelae in the form of sensory and nervous disorders, such as ataxia and choreiform movements, blindness and other paralyses of the special senses, psychoses, peripheral neuritis, and kidney damage, are not unusual.

The symptoms of chronic poisoning are similar but milder. In addition to the digestive and sensory disturbances, there may be neurological manifestations such as incoordination and paralysis of the extremities, encephalitis, endocrine disorders, psychoses, and epilation.

Loss of hair is the most familiar sign of thallium intoxication. It usually appears in the first 10 to 14 days of the disease, but it may not be evident in persons dying within a few days after absorption of large amounts of the poison. The mechanism of hair loss is unknown. Alopecia is fairly characteristic of thallium poisoning although it may also occur in chronic arsenic, lead, and mercury poisoning, after roentgenography and employment of radium, and after the use of certain hair preparations and drugs. It rarely occurs after acute poisoning by compounds other than thallium salts.

Little is known about the specific treatment of thallium poisoning. There is no evidence that iodides materially affect the course of poisoning once significant amounts of thallium have been absorbed. The value of sodium thiosulfate, calcium, or other agents to mobilize thallium from the tissues remains unproved. There is no basis in experimental animal evidence for the use of dimercaprol (BAL) in the treatment of thallium poisoning. Symptomatic (analgesics, sedatives) and supportive measures (physical medicine, maintenance of nutrition and fluid balance) are often required to counteract the widespread and profound alterations of vital functions which invariably occur.

Thallium poisoning in man has had a rather notorious record. This chemical has been frequently used for suicidal or homicidal purposes, and these intentional misuses are part of the justification for the strict regulation of this poison in Australia, England, France, and elsewhere. In New South Wales, Australia, the frequency of intentional poisoning has been so alarming in recent years that a ban on the importation of thallium was threatened. In Europe, thallium is now claimed to be superseding arsenic as a homicidal agent. Aside from its intrinsic efficiency for this purpose thallium is used, in part, because of easy availability and, in part, because of publicity which has accompanied its use in murders.

Therapeutic poisoning or injury from cosmetic depilatories containing thallium has largely disappeared. Industrial poisoning has always been infrequent, and only a few reports have appeared in the literature. Last year, thallium poisoning in workers impregnating grain was reported from several small industrial establishments in Sweden. Handling the powder without gloves and possible contamination of skin and clothing by liquid thallium impregnate were thought to be the causative factors in injury.

Food poisoning from the ingestion of accidentally contaminated products is occasionally reported. The first and the most widely publicized of these reports occurred in the early 1930's in California. It was associated with the ingestion of thalliferous tortillas by 31 Mexicans, 7 of whom died. More recently, in Turkey, food poisoning occurred from ingestion of bread made with thallium-containing flour thought to be contaminated by grain impregnated with this rodenticide. Contamination was sufficient to cause the death of two children and poisoning of five others. Secondary poisoning from the ingestion of the meat of a hen who had consumed poisoned grain was reported from East Germany several years ago. A Finnish report described non-fatal thallium-treated peas intended for the destruction of pigeons.

An alarming increase in the incidence of thallotoxicosis in infants and children has been reported in Texas this year. Three deaths and well over 60 serious thallium poisoning cases in small children have been recorded in the state's major population areas in a six-month period. The high incidence of poisoning is attributed to the easy accessibility and availability of ant and rodent poisons containing thallium, which are prepared and packaged in a manner especially attractive to children. The problem is not peculiar to Texas, however. Similar cases have been reported from New York to Oregon but with greatest frequency from the southwest and western states.

Thallium is used in these areas principally as an insecticide and rodenticide in the form of a sirup, jelly, and paste for use alone, or it is applied to foods such as bread and cake crumbs, chocolate, peanut butter, nuts, and cereal grains. Homemade and ready-made poison baits containing 1 to 5% of thallium are dispensed alone or in makeshift containers such as bottle caps or short sections of soda straws. The sweetness or savoriness of the bait, coupled with the attractiveness and availability of the bait container or carrier, contributes to the hazards of this material, especially for small children and household pets. Efforts, short of legislation, to encourage more careful distribution and to modify formulations and packaging to make pesticides containing thallium less appetizing and attractive to children have met with little success. One Texas city banned the general sale of insecticides containing 3% or more of thallium. An injunction against marketing these products was threatened at the state level.

When thallium products are needed for the control of highly resistant species of insects and rodents, they should be subject to the type of restriction invoked for very dangerous substances, namely, use by experienced personnel familiar with its hazards and trained in its handling. This recommendation is neither new nor novel. Over 30 years ago, a similar recommendation was made in THE JOURNAL in an early review of the hazards of thallium used in agriculture. The intervening years have provided ample evidence to support the wisdom of the recommendation.

J.A.M.A. 165:1566 (Nov. 23) 1957.

POSITIONS

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CHIEF PHARMACIST—prefer general hospital in Florida; registered in Ohio and Florida; experienced in both hospital and retail pharmacy. PW-12.

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CHIEF PHARMACIST—prefer Minnesota or California, with registration in those states; ten years' experience with government service, including commissions in U. S. Public Health Service and in the Navy; experience with the Veterans' Administration as Chief Pharmacist; Pharm. D. degree. PW-15.

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